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(FILE 'HOME' ENTERED AT 06:53:55 ON 22 OCT 2002)
SET COST OFF

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

FILE 'REGISTRY' ENTERED AT 06:55:37 ON 22 OCT 2002

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L1      1 S 143011-72-7
L2      4 S 163042-96-4 OR 152918-27-9 OR 152918-18-8 OR 89705-21-5
        ACT YOUNG832/A
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L3 (      86)SEA FILE=HCAPLUS ABB=ON PLU=ON ("FISHMAN P"/AU OR "FISHMAN P
L4 (      7)SEA FILE=HCAPLUS ABB=ON PLU=ON ("CAN FITE BIOPHARMA LTD"/PA O
L5 (     88)SEA FILE=HCAPLUS ABB=ON PLU=ON (L3 OR L4)
L6 (     34)SEA FILE=HCAPLUS ABB=ON PLU=ON AB MECA
L7 (    139)SEA FILE=HCAPLUS ABB=ON PLU=ON IB MECA
L8 (     40)SEA FILE=HCAPLUS ABB=ON PLU=ON CL IB MECA
L9 (    341)SEA FILE=HCAPLUS ABB=ON PLU=ON "ADENOSINE RECEPTORS (L) A3"/C
L10 (   707)SEA FILE=HCAPLUS ABB=ON PLU=ON ADENOSIN?(L)A3(L)RECEPTOR
L11 (   261)SEA FILE=HCAPLUS ABB=ON PLU=ON ("RECEPTORS (L) PURINERGIC P1"
L12 (   280)SEA FILE=HCAPLUS ABB=ON PLU=ON "ADENOSINE RECEPTORS"/CT(L)AGO
L13 (  4518)SEA FILE=HCAPLUS ABB=ON PLU=ON ADENOSIN?(L)RECEPTOR(L)AGONIST
L14 (   429)SEA FILE=HCAPLUS ABB=ON PLU=ON ADENOSIN?(L)RECEPTOR(L)AGONIST
L15 (    15)SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND (L6 OR L7 OR L8 OR L9 O
L16 (     4)SEA FILE=REGISTRY ABB=ON PLU=ON 89705-21-5 OR 152918-27-9 OR
L17 (     1)SEA FILE=REGISTRY ABB=ON PLU=ON 120-73-0
L18 (     1)SEA FILE=REGISTRY ABB=ON PLU=ON 58-61-7
L19 (   138)SEA FILE=HCAPLUS ABB=ON PLU=ON L16
L20 (    25)SEA FILE=HCAPLUS ABB=ON PLU=ON 2 CHLORO N6 3 IODOBENZYL ADENO
L21 (    48)SEA FILE=HCAPLUS ABB=ON PLU=ON N6 3 IODOBENZYL ADENOSINE 5 N
L22 (     9)SEA FILE=HCAPLUS ABB=ON PLU=ON N6 2 4 AMINOPHENYL ETHYL ADENO
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L26 (    12)SEA FILE=HCAPLUS ABB=ON PLU=ON CI IB MECA
L27 (    56)SEA FILE=HCAPLUS ABB=ON PLU=ON A3AR
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L32 (   100)SEA FILE=REGISTRY ABB=ON PLU=ON L31 AND 333.446/RID
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L34 (    94)SEA FILE=REGISTRY ABB=ON PLU=ON L33 NOT (L17 OR L18)
L35      SEL PLU=ON L30 1- RN :      78 TERMS
L36 (    78)SEA FILE=REGISTRY ABB=ON PLU=ON L35
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L41 (   96506)SEA FILE=REGISTRY SSS FUL L40
L42      STR
L43 (   69707)SEA FILE=REGISTRY SUB=L41 CSS FUL L42
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L46 (    94)SEA FILE=REGISTRY ABB=ON PLU=ON L45 NOT 58-55-9
L47 (    93)SEA FILE=REGISTRY ABB=ON PLU=ON L46 NOT 118-00-3
L48 (    84)SEA FILE=REGISTRY ABB=ON PLU=ON L47 NOT GUANOS?
L49 (    47)SEA FILE=REGISTRY ABB=ON PLU=ON L48 AND L43
L50 (    37)SEA FILE=REGISTRY ABB=ON PLU=ON L48 NOT L49
L51 (    19)SEA FILE=REGISTRY ABB=ON PLU=ON L41 AND L50
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        ACT YOUNG832A/A
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L53 ( 181680)SEA FILE=REGISTRY ABB=ON PLU=ON 333.446/RID
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L55 56975 SEA FILE=REGISTRY SUB=L53 CSS FUL L54
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L57 STR
L58 ( 56975)SEA FILE=REGISTRY SUB=L56 CSS FUL L57
L59 STR
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L63 ( 56975)SEA FILE=REGISTRY SUB=L61 CSS FUL L62
L64 STR
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ACT YOUNG832E/A
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L71 STR
L72 ( 47535)SEA FILE=REGISTRY SUB=L70 CSS FUL L71
L73 STR
L74 ( 10896)SEA FILE=REGISTRY SUB=L72 CSS FUL L73
L75 STR
L76 ( 10891)SEA FILE=REGISTRY SUB=L74 CSS FUL L75
L77 STR
L78 843 SEA FILE=REGISTRY SUB=L76 CSS FUL L77
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ACT YOUNG832F/A
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L83 ( 47535)SEA FILE=REGISTRY SUB=L81 CSS FUL L82
L84 STR
L85 ( 10896)SEA FILE=REGISTRY SUB=L83 CSS FUL L84
L86 STR
L87 ( 10891)SEA FILE=REGISTRY SUB=L85 CSS FUL L86
L88 STR
L89 ( 843)SEA FILE=REGISTRY SUB=L87 CSS FUL L88
L90 ( 744)SEA FILE=REGISTRY ABB=ON PLU=ON L89 NOT (PMS OR MNS OR IDS)/C
L91 ( 640)SEA FILE=REGISTRY ABB=ON PLU=ON L90 NOT COMPD
L92 ( 582)SEA FILE=REGISTRY ABB=ON PLU=ON L91 NOT SQL/FA
L93 ( 75)SEA FILE=REGISTRY ABB=ON PLU=ON L92 AND NC>=2
L94 ( 42)SEA FILE=REGISTRY ABB=ON PLU=ON L93 NOT MXS/CI
L95 ( 27)SEA FILE=REGISTRY ABB=ON PLU=ON L94 NOT 58-61-7/CRN
L96 ( 507)SEA FILE=REGISTRY ABB=ON PLU=ON L92 NOT L93
L97 ( 506)SEA FILE=REGISTRY ABB=ON PLU=ON L96 NOT 58-61-7
L98 ( 417)SEA FILE=REGISTRY ABB=ON PLU=ON L97 NOT (11C# OR 13C# OR 14C#
L99 444 SEA FILE=REGISTRY ABB=ON PLU=ON (L95 OR L98)
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L100 444 S L99 NOT (58-55-9 OR 118-00-3 OR 958-09-8)

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L101 4269 S L1
 L102 7004 S (G OR GRANULOCYT?) () (CSF OR COLON? STIMULAT? FACTOR)
 L103 7098 S L101,L102
 L104 138 S L2
 L105 52 S (CL OR CI) () IB MECA
 L106 139 S IB MECA
 L107 34 S AB MECA
 L108 1501 S APNEA NOT SLEEP?
 L109 25 S 2 CHLORO () (N6 OR N 6) () 3 IODOBENZ? ADENOSIN? 5 N METHYLURON
 L110 48 S (N6 OR N 6) () 3 IODOBENZ? ADENOSIN? 5 N METHYLURONAMIDE
 L111 49 S (N6 OR N 6) () 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADENOS
 L112 7 S (N6 OR N 6) () 4 AMINO 3 IODOBENZ? ADENOSIN? 5 N METHYLURONAMID
 L113 1 S N 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADENOSIN?)
 L114 49 S (N6 OR N 6) () 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADEN
 L115 0 S 6 N 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADENOSIN?)
 L116 108 S A3AR OR A2AR OR A3AR
 L117 11994 S ADENOSIN?(L) RECEPTOR?
 E ADENOSINE RECEPTOR/CT
 L118 2069 S E6,E7,E8,E9,E10
 L119 46 S A2AAR OR A2BAR
 E E5+ALL
 L120 4563 S E8,E7+NT
 L121 4 S L103 AND L104-L115
 L122 18 S L103 AND L116-L120
 E LEUKOPEN
 L123 3002 S E4-E9,E12
 E LEUCOPEN
 L124 1037 S E4-E7,E11
 E LEUKOCYTOPEN
 L125 970 S E2,E4,E5,E8
 E LEUCOCYTOPEN
 L126 28 S E4
 E LEUKOCYTOPEN/CT
 E E4+ALL
 L127 807 S E3
 L128 3392 S E3/BI OR E4/BI OR E5/BI OR E6/BI
 L129 164 S L103 AND L123-L128
 L130 3 S L121,L122 AND L129
 E BONE MARROW/CT
 E E3+ALL
 L131 21852 S E16+NT
 L132 51298 S E16/BI
 E E20+ALL
 L133 31615 S E6+NT
 E E30+ALL
 E E22+ALL
 L134 19391 S E4,E3+NT
 L135 16238 S E3/BI
 E E10+ALL
 L136 22302 S E5+NT
 E E29+ALL
 L137 1555 S E4
 E E13+ALL
 L138 2838 S E5,E6,E4+NT
 L139 9 S L104-L115 AND L123-L129
 L140 13 S L104-L115 AND L131-L138
 L141 129 S L116-L120 AND L123-L128,L131-L138
 L142 5496 S L52,L60,L99

FILE 'REGISTRY' ENTERED AT 07:16:53 ON 22 OCT 2002

L143 10433 S L67,L78 NOT L52,L60,L99
 L144 10432 S L143 NOT (58-55-9 OR 118-00-3 OR 958-09-8 OR 58-61-7)
 L145 10431 S L144 NOT 53-84-9

L146 2046 S L145 NOT (P/ELS OR SQL/FA OR (PMS OR MNS OR MXS OR IDS)/CI)

FILE 'HCAPLUS' ENTERED AT 07:18:29 ON 22 OCT 2002

L147 5695 S L146
L148 10759 S L142,L147
L149 57 S L148 AND L103
L150 2126 S L148 AND L116-L120
L151 335 S L148 AND L123-L128,L131-L138
L152 18 S L150 AND L151
L153 37 S L149 AND L150,L151
L154 4 S L152 AND L153
L155 36 S L121,L122,L130,L139,L140,L154
L156 53 S L149,L153 NOT L155
L157 114 S L141 NOT L155,L156
E CAN/CS,PA
E CAN-FIT/CS,P
E CAN-FIT/CS,PA
E CAN FIT/CS,PA
L158 7 S E5-E10
E FISHMAN P/AU
L159 86 S E3-E6,E15
L160 6 S L158,L159 AND L103
L161 6 S L160 AND L155-L157
L162 136 S L155-L157 AND (PD<=19990910 OR PRD<=19990910 OR AD<=19990910)
L163 26 S L155 AND L162
L164 6 S L163 AND (HEMATOPO? OR CANCER OR BONE MARROW OR CELL PROLIFER
L165 25 S L162 AND L156
L166 15 S L165 AND (MARROW OR RANDOMIZ? OR MYELO? OR LEUKEM?)/TI
L167 8 S L166 NOT FLAG/TI
SEL DN AN 2 3 5 8
L168 4 S L167 NOT E1-E12
L169 13 S L161,L164,L168
L170 85 S L162 NOT L163-L169
L171 34 S L170 AND (1 OR 15 OR 63)/SC
L172 13 S L171 AND (MAST CELL OR PROLIFERAT? OR HEMATOPO? OR EXPANSION
SEL DN AN 1 3
L173 6 S E3-E18
L174 19 S L169,L173 AND L101-L142,L147-L173
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 07:39:39 ON 22 OCT 2002

L175 11 S E19-E29
L176 1 S L175 AND L1
L177 10 S L175 NOT L176

=> fil reg

FILE 'REGISTRY' ENTERED AT 07:40:25 ON 22 OCT 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 20 OCT 2002 HIGHEST RN 463296-69-7
DICTIONARY FILE UPDATES: 20 OCT 2002 HIGHEST RN 463296-69-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d ide can 1176

L176 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 143011-72-7 REGISTRY
CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)
OTHER NAMES:
CN G-CSF
CN Granocyte
CN Granulocyte colony-stimulating factor
MF Unspecified
CI COM, MAN
SR CA
LC STN Files: BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS,
CIN, MEDLINE, MRCK*, PHAR, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

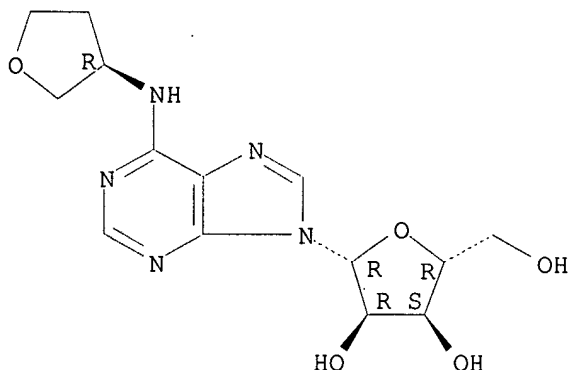
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4262 REFERENCES IN FILE CA (1962 TO DATE)
105 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4269 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:253043
REFERENCE 2: 137:246548
REFERENCE 3: 137:246329
REFERENCE 4: 137:246314
REFERENCE 5: 137:246133
REFERENCE 6: 137:244062
REFERENCE 7: 137:241838
REFERENCE 8: 137:241829
REFERENCE 9: 137:241731
REFERENCE 10: 137:237705

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L177 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN 204512-90-3 REGISTRY
CN Adenosine, N-[(3R)-tetrahydro-3-furanyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CVT 510
CN Tecadenoson
FS STEREOSEARCH
DR 343921-68-6
MF C14 H19 N5 O5
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, DRUGNL, DRUGPAT,
DRUGUPDATES, PHAR, SYNTHLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



Handwritten: HIV compounds for
ref 1-19, set L174

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1962 TO DATE)
14 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:163189
REFERENCE 2: 136:257289
REFERENCE 3: 136:241669
REFERENCE 4: 136:128795
REFERENCE 5: 135:266911
REFERENCE 6: 135:132114
REFERENCE 7: 135:33626
REFERENCE 8: 135:19874
REFERENCE 9: 135:19873
REFERENCE 10: 135:5771

L177 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 163042-96-4 REGISTRY

CN .beta.-D-Ribofuranuronamide, 1-[2-chloro-6-[[[3-iodophenyl)methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2-Chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide

CN C1-IB-MECA

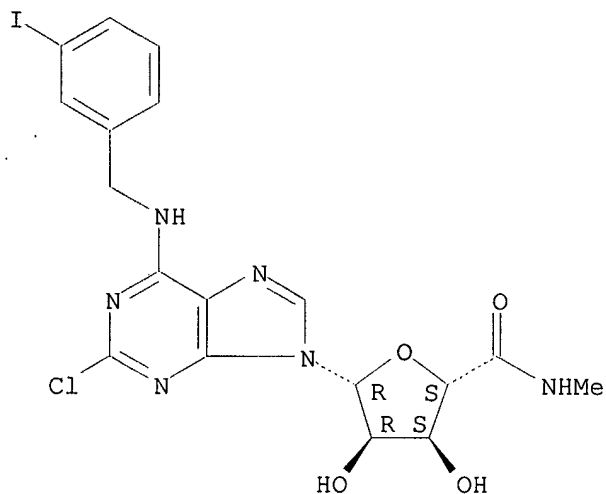
FS STEREOSEARCH

MF C18 H18 Cl I N6 O4

SR CA

LC STN Files: ADISINSIGHT, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM,
MEDLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

43 REFERENCES IN FILE CA (1962 TO DATE)
43 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:163843
REFERENCE 2: 137:136577
REFERENCE 3: 137:88436
REFERENCE 4: 136:380449
REFERENCE 5: 136:319688
REFERENCE 6: 136:273473
REFERENCE 7: 136:272934
REFERENCE 8: 136:257615
REFERENCE 9: 136:242084
REFERENCE 10: 136:161304

L177 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN **152918-27-9** REGISTRY

CN .beta.-D-Ribofuranuronamide, 1-[6-[[[4-amino-3-iodophenyl)methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN AB-MECA

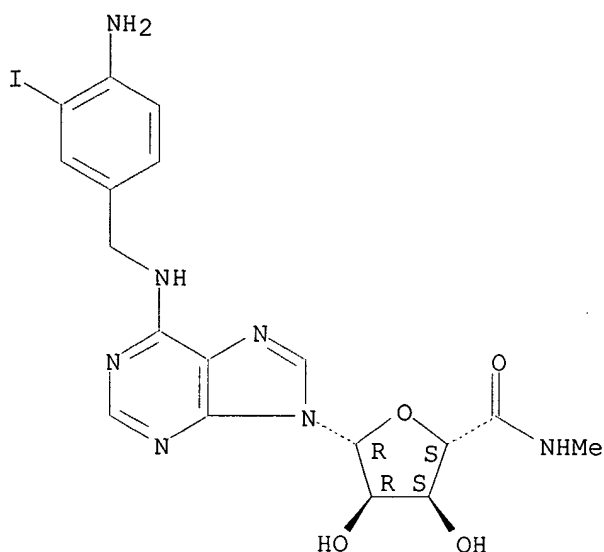
FS STEREOSEARCH

MF C18 H20 I N7 O4

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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20 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 2: 137:136577

REFERENCE 3: 137:88436

REFERENCE 4: 136:380449

REFERENCE 5: 136:48571

REFERENCE 6: 134:231860

REFERENCE 7: 133:261543

REFERENCE 8: 130:20187

REFERENCE 9: 130:10309

REFERENCE 10: 129:228699

L177 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN **152918-18-8** REGISTRY

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-[6-[[[(3-iodophenyl)methyl]amino]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN IB-MECA

CN N6-(3-Iodobenzyl)adenosine-5'-N-methyluronamide

FS STEREOSEARCH

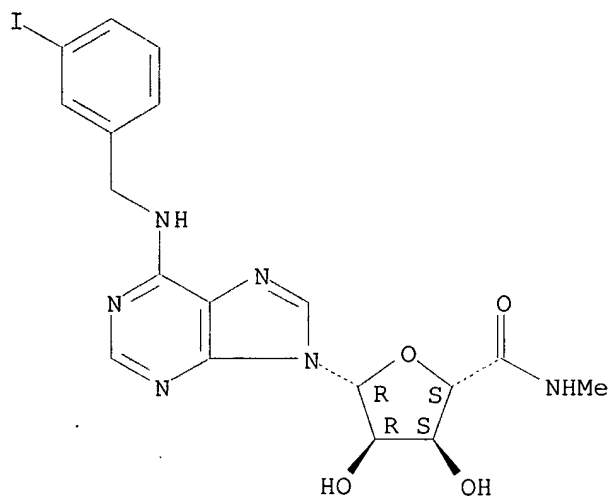
DR 215462-30-9

MF C18 H19 I N6 O4

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CSCHEM, MEDLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



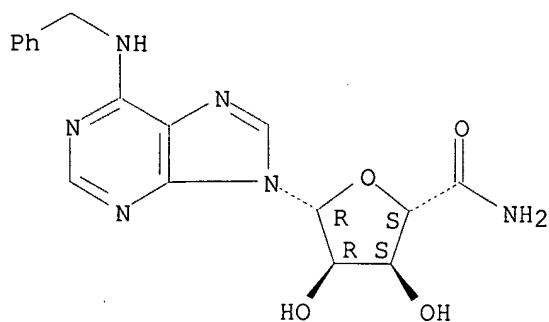
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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75 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 4: 137:88436
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REFERENCE 6: 136:380449
REFERENCE 7: 136:365554
REFERENCE 8: 136:350750
REFERENCE 9: 136:161304
REFERENCE 10: 136:145239

L177 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN 152918-14-4 REGISTRY
CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H18 N6 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1962 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 5 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:88436
 REFERENCE 2: 134:231860
 REFERENCE 3: 129:109311
 REFERENCE 4: 124:225
 REFERENCE 5: 120:289415

L177 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN **120442-40-2** REGISTRY

CN Adenosine, N-[2-(3,5-dimethoxyphenyl)-2-(2-methylphenyl)ethyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN CGS 24012

CN DPMA

CN PD 125944

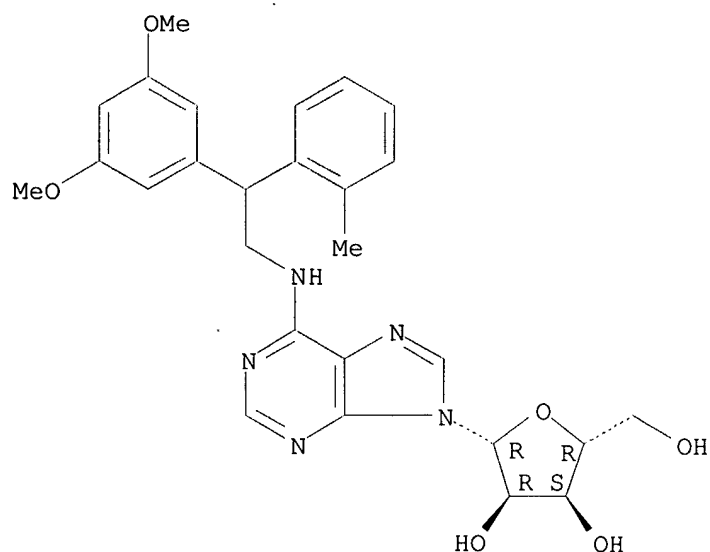
FS STEREOSEARCH

MF C27 H31 N5 O6

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, MEDLINE, PIRA, TOXCENTER, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

44 REFERENCES IN FILE CA (1962 TO DATE)
44 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 2: 135:221151
REFERENCE 3: 135:162508
REFERENCE 4: 135:43868
REFERENCE 5: 134:231860
REFERENCE 6: 134:217113
REFERENCE 7: 134:110841
REFERENCE 8: 133:359476
REFERENCE 9: 133:217854
REFERENCE 10: 130:247042

L177 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN **41552-82-3** REGISTRY

CN Adenosine, N-cyclopentyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN CPA

CN N-Cyclopentyladenosine

CN N6-cyclopentyladenosine

CN N6-Cyclopentyladenosine

CN UK 80882

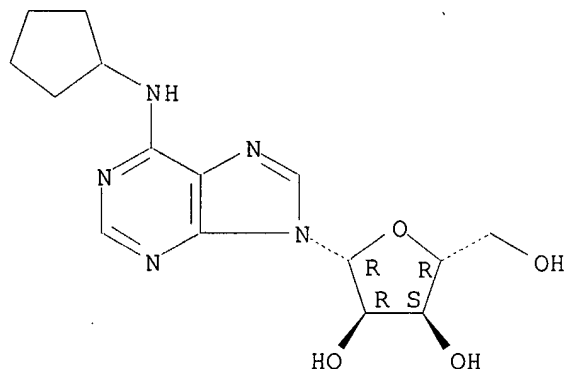
FS STEREOSEARCH

MF C15 H21 N5 O4

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU,
DRUGU, EMBASE, IPA, MEDLINE, MSDS-OHS, TOXCENTER, USPATFULL

(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

469 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
469 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:243504
REFERENCE 2: 137:217173
REFERENCE 3: 137:211198
REFERENCE 4: 137:210830
REFERENCE 5: 137:195896
REFERENCE 6: 137:163843
REFERENCE 7: 137:150526
REFERENCE 8: 137:150259
REFERENCE 9: 137:135364
REFERENCE 10: 137:134944

L177 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 37739-05-2 REGISTRY

CN Adenosine, 2-chloro-N-cyclopentyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2-Chloro-N6-cyclopentyladenosine

CN 2-Chloro-N6-cyclopentyladenosine

CN CCPA

FS STEREOSEARCH

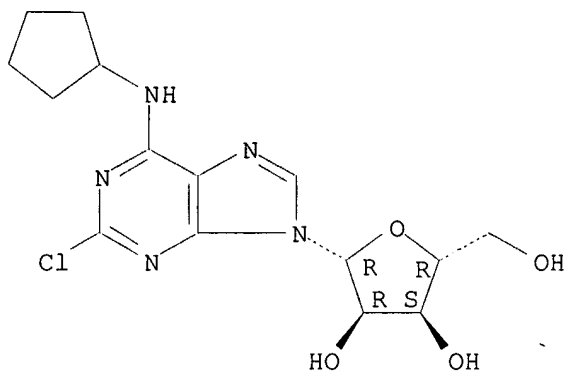
DR 172613-66-0

MF C15 H20 Cl N5 O4

LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT,
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PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USPATFULL

(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

139 REFERENCES IN FILE CA (1962 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 139 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:226896
 REFERENCE 2: 137:164033
 REFERENCE 3: 137:119953
 REFERENCE 4: 137:103775
 REFERENCE 5: 137:28514
 REFERENCE 6: 136:319688
 REFERENCE 7: 136:257616
 REFERENCE 8: 136:257289
 REFERENCE 9: 136:145101
 REFERENCE 10: 136:15094

L177 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 36396-99-3 REGISTRY

CN Adenosine, N-cyclohexyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN CHA

CN Cyclohexyladenosine

CN N-Cyclohexyladenosine

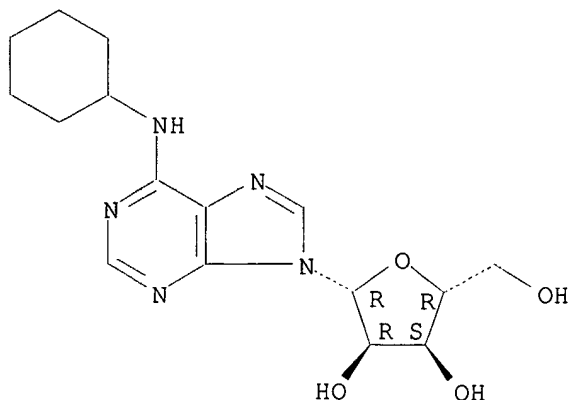
CN N6-Cyclohexyladenosine

FS STEREOSEARCH

MF C16 H23 N5 O4

LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
 CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE,
 MEDLINE, MSDS-OHS, TOXCENTER, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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 5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 570 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:163843

REFERENCE 2: 137:163757

REFERENCE 3: 137:103775

REFERENCE 4: 137:88259

REFERENCE 5: 137:18547

REFERENCE 6: 136:335498

REFERENCE 7: 136:257289

REFERENCE 8: 136:226629

REFERENCE 9: 136:217007

REFERENCE 10: 136:177829

L177 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 21679-14-1 REGISTRY

CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Adenine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (8CI)

OTHER NAMES:

CN 2-Fluoro-9-.beta.-D-arabinofuranosyladenine

CN 9-.beta.-D-Arabinofuranosyl-2-fluoroadenine

CN 9-.beta.-D-Arabinosyl-2-fluoroadenine

CN F-ara-A

CN Fludarabine

CN NSC 118218

CN NSC 118218H

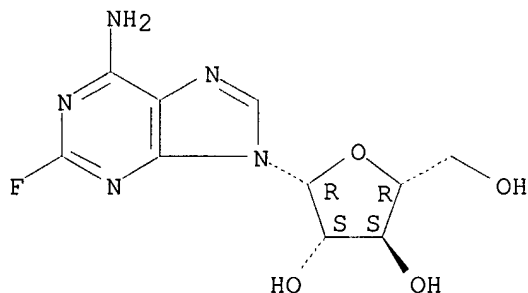
FS STEREOSEARCH

MF C10 H12 F N5 O4

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER,

USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

530 REFERENCES IN FILE CA (1962 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
532 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 10: 137:215809

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=> d all hitstr tot 1174

L174 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:469221 HCAPLUS

TI A3 **adenosine receptor** as a target for cancer therapy

AU **Fishman, Pnina**; Bar-Yehuda, Sara; Madi, Lea; Cohn, Ilan

CS Laboratory of Clinical and Tumor Immunology, The Felsenstein Medical Research Center, Rabin Medical Center, Tel-Aviv University, Petach Tikva, 49100, Israel

SO Anti-Cancer Drugs (2002), 13(5), 437-443

CODEN: ANTDEV; ISSN: 0959-4973

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 1 (Pharmacology)

AB Targeting the A3 **adenosine receptor** (A3AR)

by **adenosine** or a synthetic agonist to this **receptor** (**IB-MECA** and **CI-IB-MECA**)

results in a differential effect on tumor and on normal cells. Both the **adenosine** and the agonists inhibit the growth of various tumor cell types such as melanoma, colon or prostate carcinoma and lymphoma.

This effect is specific and is exerted on tumor cells only. Moreover, exposure of peripheral blood mononuclear cells to **adenosine** or the agonists leads to the induction of **granulocyte**

colony stimulating factor (G-

CSF) prodn. When given orally to mice, the agonists suppress the growth of melanoma, colon and prostate carcinoma in these animals, while inducing a myeloprotective effect via the induction of G-

CSF prodn. The de-regulation of the Wnt signaling pathway was

found to be involved in the anticancer effect. **Receptor**

activation induces inhibition of adenylyl cyclase with a subsequent decrease in the level of protein kinase A and protein kinase B/Akt leading to activation of glycogen synthase kinase-3.beta., a key element in the Wnt pathway. The oral bioavailability of the synthetic **A3AR**

agonists, and their induced systemic anticancer and myeloprotective effect, renders them potentially useful in three different modes of treatment: as a standalone anticancer treatment, in combination with chemotherapy to enhance its therapeutic index and myelprotection. It is evident that use of the **A3AR** agonist for increasing the therapeutic index of chemotherapy may also invariably give rise to myelprotection and vice versa. The **A3AR** agonists are thus a promising new class of agents for cancer therapy.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bar-Yehuda, S; Clin Exp Metast 1999, V17, P531 HCAPLUS

(2) Bar-Yehuda, S; Neoplasia 2001, V3, P125 HCAPLUS

(3) Bowlin, T; Cell Mol Biol 1997, V43, P345 HCAPLUS

(4) Djaldetti, M; Clin Exp Metast 1996, V14, P189 HCAPLUS

- (5) Fishman, P; Cancer Res 1998, V58, P3181 HCAPLUS
- (6) Fishman, P; Cancer Res 1998, V58, P3181 HCAPLUS
- (7) Fishman, P; Eur J Cancer 2000, V36, P1452 HCAPLUS
- (8) Fishman, P; J Cell Physiol 2000, V183, P393 HCAPLUS
- (9) Fishman, P; Oncogene, in press 2002
- (10) Gessi, S; Br J Pharmacol 2001, V134, P116 HCAPLUS
- (11) Jacobson, K; Drugs Fut 1995, V20, P689
- (12) Jacobson, K; J Biol Chem 2000, V275, P30272 HCAPLUS
- (13) Liu, G; Cardiovasc Res 1994, V28, P1057 HCAPLUS
- (14) Merighi, S; Br J Pharmacol 2001, V134, P1215 HCAPLUS
- (15) Olah, M; Pharmacol Ther 2000, V85, P55 HCAPLUS
- (16) Palmer, T; Mol Pharmacol 1997, V52, P632 HCAPLUS
- (17) Palmer, T; Mol Pharmacol 2000, V57, P539 HCAPLUS
- (18) Poulsen, S; Bioorg Med Chem 1998, V6, P619 HCAPLUS
- (19) Shneyvays, V; J Mol Cell Cardiol 2001, V33, P1249 HCAPLUS
- (20) Suh, B; Br J Pharmacol 2001, V134, P132 HCAPLUS
- (21) Trincavelli, M; J Neurochem 2000, V75, P1493 HCAPLUS
- (22) Von Lubitz, D; Ann NY Acad Sci 2001, V939, P85 HCAPLUS
- (23) Zhao, Z; Microvasc Res 2002, V63, P61 HCAPLUS

L174 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:241343 HCAPLUS

DN 136:257289

TI Pharmaceutical use of adenosine agonists for inducing **bone marrow cell proliferation**

IN Fishman, Pnina; Cohn, Ilan

PA Israel

SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 782,259.
CODEN: USXXCO

DT Patent

LA English

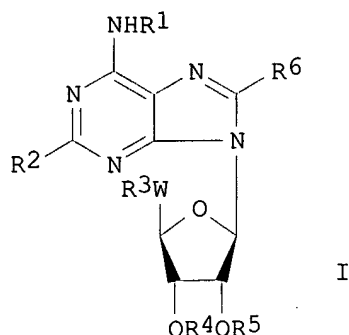
IC ICM A61K031-7076

NCL 514046000

CC 1-12 (Pharmacology)

FAN.CNT 3

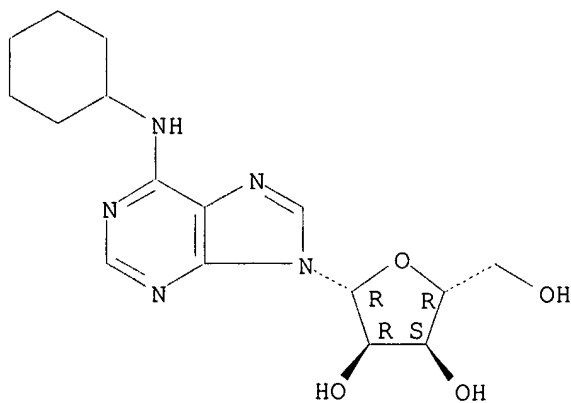
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	WO 2000040251	A1	20000713	WO 2000-IL14	20000107	<--
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	RW:					GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
	US 2001031742	A1	20011018	US 2001-782259	20010214	<--
PRAI	IL 1999-127947	A	19990107			<--
	WO 2000-IL14	W	20000107			
	US 2001-700744	A2	20010109			✓
	US 2001-782259	A2	20010214			
OS	MARPAT 136:257289					
GI						



- AB The present invention relates to a method for inducing proliferation of the hematopoietic system, in particular, of **bone marrow** cells, comprising administering to a subject an effective amt. of an **adenosine A1 receptor** agonist. The method of the invention may be utilized in a variety of clin. situations where such proliferation is therapeutically beneficial. The active ingredient within the pharmaceutical compn. of the invention may be a compd. of general formula I (R1 represents a lower alkyl, substituted or unsubstituted cycloalkyl, hydroxy or hydroxyalkyl, etc.; R2 represents hydrogen, halogen, substituted or unsubstituted lower alkyl or alkenyl, lower haloalkyl or alkenyl cyano, etc.; W represents the group -OCH2-, -NHCH2-, -SCH2- or -NH(C:O)-; R3, R4 and R5 represent independently hydrogen, lower alkyl or lower alkenyl, branched or unbranched C1-C12alkanoyl, benzoyl or substituted benzoyl, etc.; and R6 represents a hydrogen or halogen atom) or any other compd. or substance which specifically binds to and/or activates the A1 **adenosine receptor** and acts as an agonist to the **receptor's** natural ligand.
- ST **adenosine A1** agonist **bone marrow** cell proliferation induction; **leukopenia** prevention **adenosine A1 receptor** agonist; **hematopoiesis** induction **adenosine A1 receptor** agonist
- IT Purinoceptor agonists
(A1; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT **Adenosine receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A1; **adenosine** agonists for inducing **bone marrow** cell proliferation)
- IT **Bone marrow**
Cell proliferation
Drug interactions
Leukocytopenia
(adenosine agonists for inducing **bone marrow** cell proliferation)
- IT Toxicity
(drug, **leukopenia** in; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT **Hematopoiesis**
(induction of; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT Antipsychotics
Antitumor agents
Chemotherapy
Radiotherapy
Tranquilizers
(**leukopenia** from; adenosine agonists for inducing **bone marrow** cell proliferation)

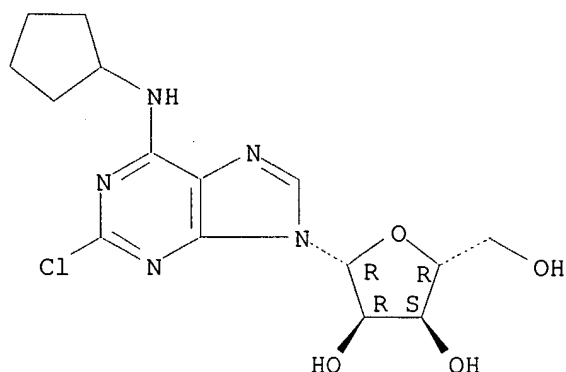
- IT Neoplasm
(**leukopenia** in; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT Agranulocytosis
(neutropenia; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT 58-61-7D, Adenosine, derivs. **36396-99-3**, Adenosine, N-cyclohexyl- **37739-05-2**, 2-Chloro-N6-cyclopentyladenosine **41552-82-3**, N6-Cyclopentyladenosine **204512-90-3**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine agonists for inducing **bone marrow** cell proliferation)
- IT **143011-72-7, G-CSF**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(induction of; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT 50-18-0, Cyclophosphamide
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**leukopenia** from; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT **36396-99-3**, Adenosine, N-cyclohexyl- **37739-05-2**, 2-Chloro-N6-cyclopentyladenosine **41552-82-3**, N6-Cyclopentyladenosine **204512-90-3**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine agonists for inducing **bone marrow** cell proliferation)
- RN 36396-99-3 HCAPLUS
CN Adenosine, N-cyclohexyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



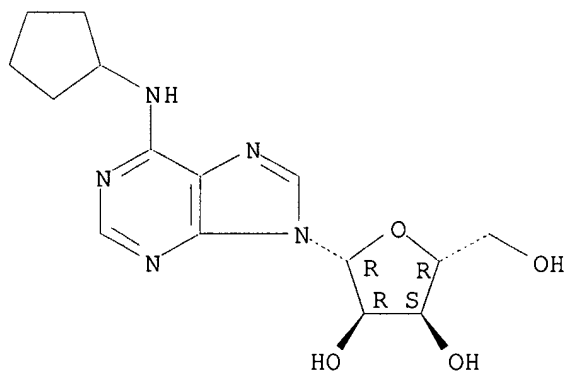
- RN 37739-05-2 HCAPLUS
CN Adenosine, 2-chloro-N-cyclopentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



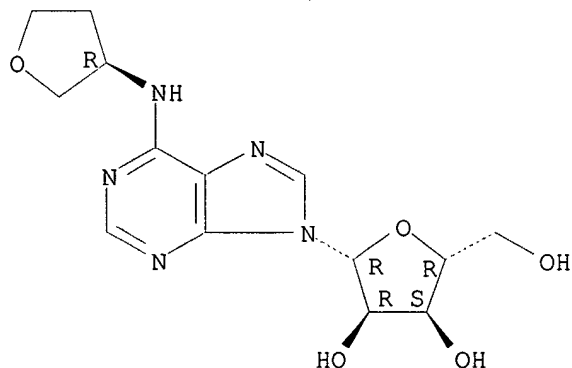
RN 41552-82-3 HCAPLUS
 CN Adenosine, N-cyclopentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204512-90-3 HCAPLUS
 CN Adenosine, N-[(3R)-tetrahydro-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 143011-72-7, G-CSF
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (induction of; adenosine agonists for inducing **bone marrow** cell proliferation)
 RN 143011-72-7 HCAPLUS
 CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:763522 HCAPLUS

DN 135:283233

TI Pharmaceutical use of adenosine agonists for inducing **bone marrow cell proliferation**

IN **Fishman, Pnina**; Cohn, Ilan

PA Israel

SO U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 700,744.

CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-7105

NCL 514045000

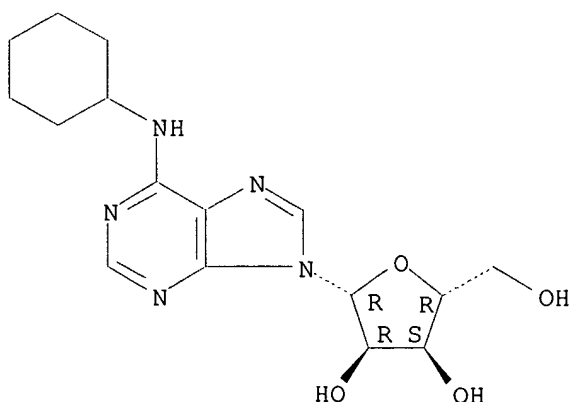
CC 1-12 (Pharmacology)

FAN.CNT 3

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	WO 2000040251	A1	20000713	WO 2000-IL14	20000107 <--
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	IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				
	MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,				
	SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,				
	AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,				
	DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,				
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PRAI	IL 1999-127947	A	19990107 <--		
	WO 2000-IL14	P	20000107		
	US 2001-700744	A2	20010109		
	US 2001-782259	A2	20010214		
OS	MARPAT 135:283233				
AB	A method is provided for inducing proliferation of bone marrow cells in a subject, comprising administering an effective amt. of an adenosine A1 receptor agonist. Also provided is a method for preventing redn. in level of leukocytes in a subject as a result of a treatment comprising administering to the individual an effective amt. of an adenosine A1 receptor agonist. In addn., the invention provides a method of treatment of an individual comprising administering to the subject a therapeutic drug in combination with an adenosine A1 receptor agonist.				
ST	adenosine A1 agonist bone marrow cell proliferation induction; leukopenia prevention adenosine A1 receptor agonist				
IT	Adenosine receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (A1 ; adenosine agonists for inducing bone marrow cell proliferation)				
IT	Antipsychotics Antitumor agents Bone marrow Cell proliferation Chemotherapy Drug interactions Drugs Leukocytopenia Radiotherapy Tranquilizers				

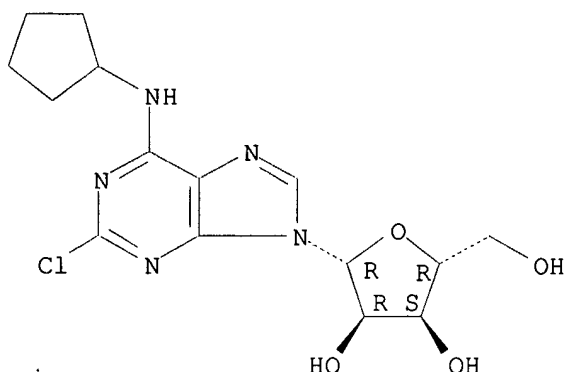
- (adenosine agonists for inducing **bone marrow** cell proliferation)
- IT Toxicity
(drug; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT Agranulocytosis
(neutropenia; adenosine agonists for inducing **bone marrow** cell proliferation)
- IT 50-18-0, Cyclophosphamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine agonists for inducing **bone marrow** cell proliferation)
- IT 58-61-7D, Adenosine, derivs., biological studies **36396-99-3**
37739-05-2, 2-Chloro-N6-cyclopentyladenosine **41552-82-3**, N6-Cyclopentyladenosine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine agonists for inducing **bone marrow** cell proliferation)
- IT **143011-72-7, G-CSF**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(adenosine agonists for inducing **bone marrow** cell proliferation)
- IT **36396-99-3 37739-05-2**, 2-Chloro-N6-cyclopentyladenosine **41552-82-3**, N6-Cyclopentyladenosine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine agonists for inducing **bone marrow** cell proliferation)
- RN 36396-99-3 HCAPLUS
CN Adenosine, N-cyclohexyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- RN 37739-05-2 HCAPLUS
CN Adenosine, 2-chloro-N-cyclopentyl- (9CI) (CA INDEX NAME)

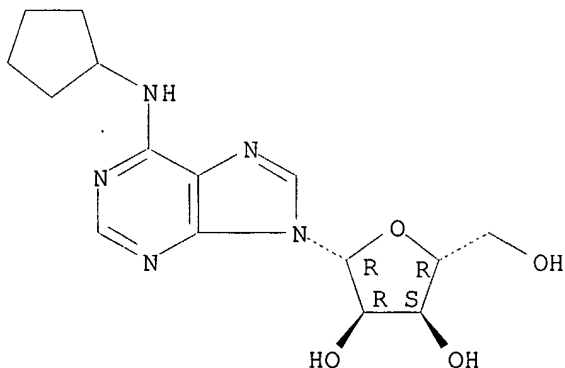
Absolute stereochemistry.



RN 41552-82-3 HCAPLUS

CN Adenosine, N-cyclopentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 143011-72-7, G-CSF

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(adenosine agonists for inducing **bone marrow** cell proliferation)

RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:698571 HCAPLUS

DN 136:144762

TI The A3 **Adenosine Receptor** as a New Target for Cancer Therapy and Chemoprotection

AU **Fishman, Pnina**; Bar-Yehuda, Sara; Barer, Faina; Madi, Lea; Multani, Asha S.; Pathak, Sen

CS Laboratory of Clinical and Tumor Immunology, The Felsenstein Medical Research Center, Rabin Medical Center, Tel-Aviv University Sackler Faculty of Medicine, Petach-Tikva, 49100, Israel

SO Experimental Cell Research (2001), 269(2), 230-236

CODEN: ECREAL; ISSN: 0014-4827

PB Academic Press

DT Journal

LA English

CC 1-6 (Pharmacology)

AB **Adenosine**, a purine nucleoside, acts as a regulatory mol., by

binding to specific G-protein-coupled A1, A2A, A2B, and A3 cell surface **receptors**. We have recently demonstrated that **adenosine** induces a differential effect on tumor and normal cells. While inhibiting in vitro tumor cell growth, it stimulates **bone marrow** cell proliferation. This dual activity was mediated through the A3 **adenosine receptor**. This study showed that a synthetic agonist to the A3 **adenosine receptor**, 2-chloro-N6-(3-iodobenzyl)-**adenosine-5'-N-methyl-uronamide** (**C1-IB-MECA**), at nanomolar concns., inhibited tumor cell growth through a cytostatic pathway, i.e., induced an increase no. of cells in the G0/G1 phase of the cell cycle and decreased the telomeric signal. Interestingly, **C1-IB-MECA** stimulates murine **bone marrow** cell proliferation through the induction of **granulocyte-colony-stimulating factor**. Oral administration of **C1-IB-MECA** to melanoma-bearing mice suppressed the development of melanoma lung metastases (60.8+/-6.5% inhibition). In combination with cyclophosphamide, a synergistic anti-tumor effect was achieved (78.5+/-9.1% inhibition). Furthermore, **C1-IB-MECA** prevented the cyclophosphamide-induced myelotoxic effects by increasing the no. of white blood cells and the percentage of neutrophils, demonstrating its efficacy as a chemoprotective agent. We conclude that A3 **adenosine receptor** agonist, **C1-IB-MECA**, exhibits systemic anticancer and chemoprotective effects. (c) 2001 Academic Press.

ST chloriodobenzyladenosinemethyluronamide cyclophosphamide antitumor **adenosine receptor** chemoprotectant cell cycle

IT Antitumor agents
Cytoprotective agents
Neutrophil

(A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT **Adenosine receptors**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(A3; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT Interphase (cell cycle)

(G0-phase; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT Interphase (cell cycle)

(G1-phase; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT Antitumor agents

(lung, metastasis; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT Antitumor agents

(melanoma; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT Lung, neoplasm

(metastasis, inhibitors; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT Drug interactions

(synergistic; A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

IT 50-18-0, Cyclophosphamide 163042-96-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(A3 **adenosine receptor** as a new target for cancer therapy and chemoprotection)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Bar-Yehuda, S; Neoplasia 2001, V3, P125 HCAPLUS

(2) Bar-Yehuda, S; Neoplasia 2001, V3, P125 HCAPLUS

- (3) Bowlin, T; Cell Mol Biol 1997, V43, P345 HCAPLUS
- (4) Brambilla, R; Naunyn-Schmiedeberg's Arch Pharmacol 2000, V361, P225 HCAPLUS
- (5) Ceruti, S; Drug Dev Res 1996, V37, P177
- (6) Fishman, P; Cancer Res 1998, V58, P3181 HCAPLUS
- (7) Fishman, P; Eur J Cancer 2000, V36, P1452 HCAPLUS
- (8) Fishman, P; J Cell Physiol 2000, V183, P393 HCAPLUS
- (9) Heine, B; Br J Ophthalmol 2000, V84, P217 MEDLINE
- (10) Ikebuchi, A; Blood 1988, V72, P2007
- (11) Itoh, Y; Int J Hematol 1992, V55, P139 MEDLINE
- (12) Jacobson, K; Drug Dev Res 1998, V45, P113 HCAPLUS
- (13) Kallassy, M; Mol Carcinog 1998, V21, P26 HCAPLUS
- (14) Krishan, A; J Cell Biol 1975, V66, P188 MEDLINE
- (15) Li, A; Bioconjugate Chem 1999, V10, P667 HCAPLUS
- (16) Li, A; J Med Chem 1999, V42, P706 HCAPLUS
- (17) Linden, J; FASEB J 1991, V5, P2668 HCAPLUS
- (18) Liu, G; Cardiovasc Res 1994, V28, P1057 HCAPLUS
- (19) Multani, A; Anticancer Res 1996, V16, P3435 MEDLINE
- (20) Multani, A; Int J Oncol 1999, V15, P423 HCAPLUS
- (21) Pathak, S; J Reprod Med 1976, V17, P25 MEDLINE
- (22) Ramirez, R; Neoplasia 1999, V1, P42 HCAPLUS
- (23) Shneyvays, V; Exp Cell Res 2000, V257, P111 HCAPLUS
- (24) Stiles, G; Clin Res 1990, V38, P10 MEDLINE
- (25) Van Schaick, E; Eur J Pharmacol 1996, V308, P311 HCAPLUS
- (26) Von Lubitz, D; Ann NY Acad Sci 1999, V890, P93 HCAPLUS
- (27) von Lubitz, D; Eur J Pharmacol 1994, V263, P59 HCAPLUS
- (28) Von Lubitz, D; Eur J Pharmacol 1995, V275, P23 HCAPLUS
- (29) Wright, W; Nat Med 2000, V8, P849
- (30) Yao, Y; Biochem Biophys Res Commun 1997, V232, P317 HCAPLUS

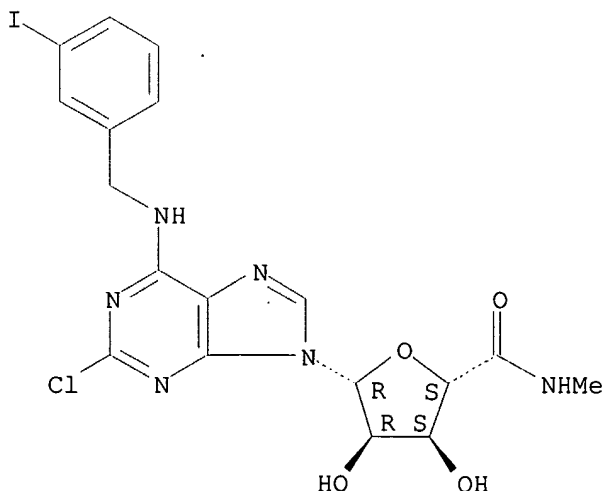
IT 163042-96-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(A3 **adenosine receptor** as a new target for cancer
therapy and chemoprotection)

RN 163042-96-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[2-chloro-6-[[3-(4-iodophenyl)methyl]amino]-
9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L174 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:208100 HCAPLUS

DN 134:231860

TI Pharmaceutical compositions comprising an **adenosine receptor** agonist or antagonist for **cancer** treatment
 IN **Fishman, Pnina**
 PA **Can-Fite Technologies Ltd., Israel**
 SO PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 ICS A61K031-7052; A61K031-7076; A61K031-708; A61K031-706; A61P039-00;
 A61P035-00
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 63

*present
application*

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001019360	A2	20010322	WO 2000-IL550	20000908 <--
	WO 2001019360	A3	20020919		
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		

PRAI IL 1999-131864 A 19990910 <--
 IL 1999-133680 A 19991223

OS MARPAT 134:231860

AB **Adenosine receptor** agonists and antagonists, particularly an agonist which binds to the A3 **adenosine receptor**, are used for induction of prodn. or secretion of **G-CSF** within the body, prevention or treatment of toxic side effects of a drug or prevention or treatment of **leukopenia**, particularly drug-induced **leukopenias**, and inhibition of abnormal cell growth and proliferation. For example, a marked inhibition of tumor growth was obsd. in nude mice with established HCT-116 human colon carcinoma treated with 5-fluorouracil (5-FU, 30 mg/kg for 5 days), 2-chloro-N6-(2-iodobenzyl)-**adenosine-5'-N-methyluronamide** (**Cl-IB-MECA**, 6 mg/kg, every other day), and the combined therapy of **Cl-IB-MECA** and 5-FU. After 20 days a clear synergistic effect between **Cl-IB-MECA** and 5-FU in noting the tumor mass was seen.

ST **adenosine receptor** agonist antagonist oral antitumor;
granulocyte colony stimulating factor
 purinoceptor antitumor

IT Purinoceptor agonists
 (A1; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)

IT **Adenosine receptors**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (A1; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)

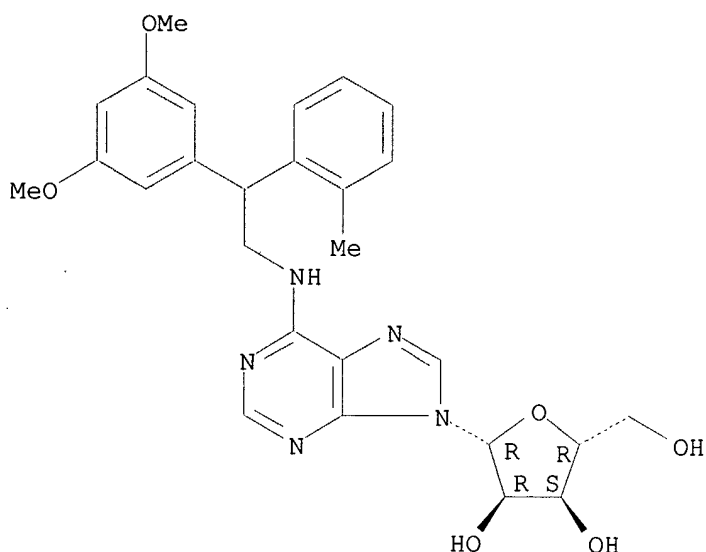
IT Purinoceptor agonists
 Purinoceptor antagonists
 (A2; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)

IT **Adenosine receptors**

- RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A2; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Purinoceptor agonists
(A3; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT **Adenosine receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A3; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Antitumor agents
(colon carcinoma; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Intestine, neoplasm
(colon, carcinoma, inhibitors; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT **Bone marrow**
Leukocyte
(differentiation and proliferation, induction of; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT **Leukocytopenia**
(drug-induced; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Body weight
(loss, drug-induced; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Antitumor agents
(lymphoma; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Antitumor agents
(melanoma; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Toxicity
(myelotoxicity, prevention of; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Antitumor agents
Cell differentiation
Cell proliferation
(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Drug delivery systems
(oral; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT Drug interactions
(synergistic; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT **Bone marrow**

- (toxicity, prevention of; oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT 51-21-8, Fluorouracil 23214-92-8, Doxorubicin
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT 120442-40-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT 58-61-7, **Adenosine**, biological studies 14114-46-6
37739-05-2, CCPA 41552-82-3, N-Cyclopentyladenosine
102146-07-6, DPCPX 152918-14-4 152918-18-8, IB
-MECA 152918-27-9, AB-MECA
163042-96-4, C1-IB-MECA
183721-15-5, MRS 1200 212329-37-8, MRS 1523
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT 143011-72-7, **Granulocyte colony-stimulating factor**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- IT 120442-40-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)
- RN 120442-40-2 HCAPLUS
CN Adenosine, N-[2-(3,5-dimethoxyphenyl)-2-(2-methylphenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 37739-05-2, CCPA 41552-82-3, N-Cyclopentyladenosine
 152918-14-4 152918-18-8, IB-MECA
 152918-27-9, AB-MECA 163042-96-4,
 C1-IB-MECA

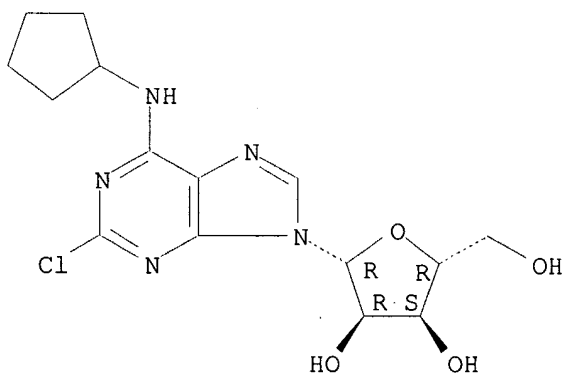
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oral compns. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)

RN 37739-05-2 HCAPLUS

CN Adenosine, 2-chloro-N-cyclopentyl- (9CI) (CA INDEX NAME)

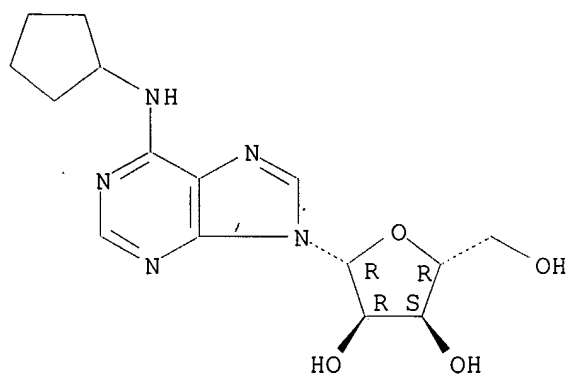
Absolute stereochemistry.



RN 41552-82-3 HCAPLUS

CN Adenosine, N-cyclopentyl- (9CI) (CA INDEX NAME)

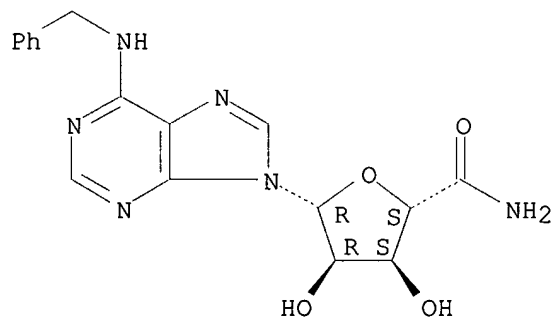
Absolute stereochemistry.



RN 152918-14-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

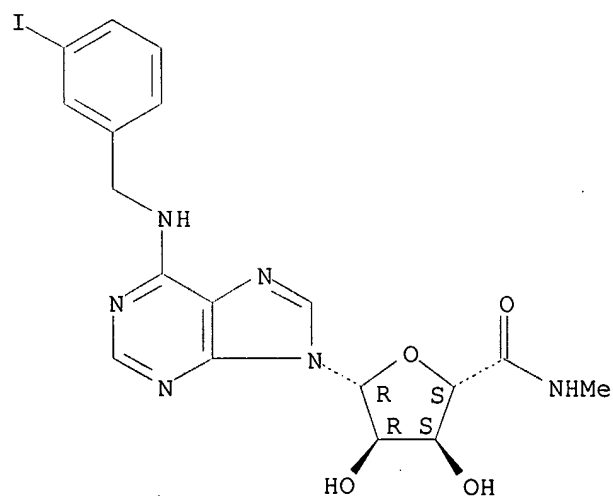
Absolute stereochemistry.



RN 152918-18-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-[6-[[[(3-iodophenyl)methyl]amino]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

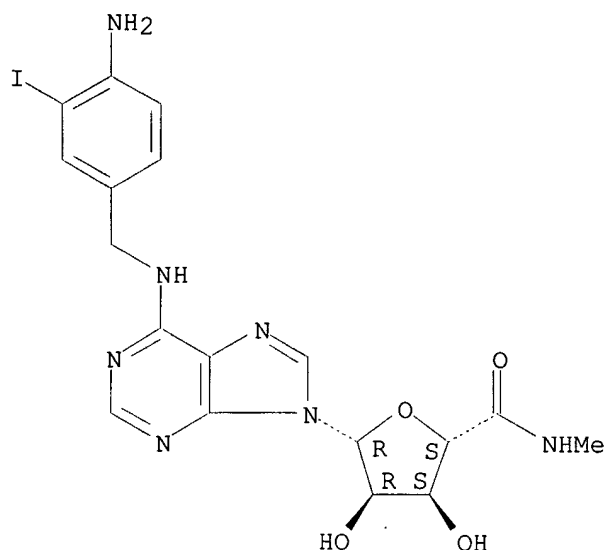


RN 152918-27-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-[[[(4-amino-3-iodophenyl)methyl]amino]-9H-

purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

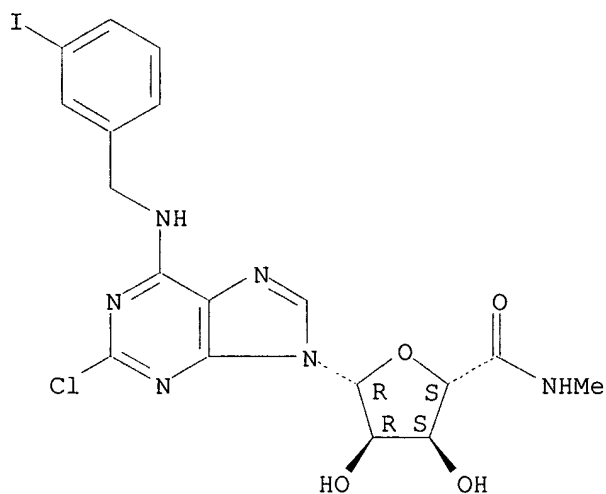
Absolute stereochemistry.



RN 163042-96-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[2-chloro-6-[(3-iodophenyl)methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 143011-72-7, **Granulocyte colony-stimulating factor**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(oral comps. comprising **adenosine receptor** agonist or antagonist for prevention or treatment of toxic side effects and cancer treatment)

RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:115003 HCAPLUS

DN 134:177357

TI Treatment of patients having non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies

IN Rastetter, William H.

PA Idec Pharmaceuticals Corporation, USA

SO PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K039-395

CC 15-3 (Immunochemistry)

Section cross-reference(s): 1, 8, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001010462	A1	20010215	WO 2000-US40459	20000725 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1207906	A1	20020529	EP 2000-965561	20000725 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	NO 2002000639	A	20020411	NO 2002-639	20020208 <--
PRAI	US 1999-148287P	P	19990811 <--		
	WO 2000-US40459	W	20000725		
AB	This invention relates to methods of reducing bone marrow involvement in B cell lymphoma patients prior to radioimmunotherapy by administering monoclonal antibodies which target cancerous B cells.				
ST	non Hodgkins lymphoma monoclonal antibody CD20; radioimmunotherapy CD20 antibody B cell lymphoma; chemotherapeutic agent monoclonal antibody CD20 lymphoma				
IT	Lymphoma (B-cell diffuse, large cell; treatment of non-Hodgkins lymphoma with bone marrow involvement with anti-CD20 antibodies)				
IT	Lymphoma (B-cell nodular; treatment of non-Hodgkins lymphoma with bone marrow involvement with anti-CD20 antibodies)				
IT	Lymphoma (B-cell; treatment of non-Hodgkins lymphoma with bone marrow involvement with anti-CD20 antibodies)				
IT	Glycoproteins, specific or class Proteins, specific or class RL: BSU (Biological study, unclassified); BIOL (Biological study) (SU (surface), B cell; treatment of non-Hodgkins lymphoma with bone marrow involvement with anti-CD20 antibodies)				
IT	Leukemia Lymphoma (T-cell; treatment of non-Hodgkins lymphoma with bone marrow involvement with anti-CD20 antibodies)				
IT	Transplant and Transplantation (bone marrow ; treatment of non-Hodgkins lymphoma with bone marrow involvement with anti-CD20 antibodies)				

IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(conjugates with anti-CD20 antibody; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphoma
(diffuse; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphocyte
(effector cell, stimulation; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized antibody; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Diagnosis
(immunodiagnosis; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Drug delivery systems
(immunotoxins; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT **Bone marrow**
(involvement; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphoma
(large cell; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphoma
(lymphoblastic; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT AIDS (disease)
(lymphoma; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Sarcoma
(lymphosarcoma; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphoma
(nodular; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphoma
(non-Hodgkin's, mantle cell; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Lymphoma
(non-Hodgkin's; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Blood
(peripheral stem cell; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Immunotherapy
(radio-; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Cell
(stem, peripheral blood; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (surface; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Platelet (blood)
 (thrombocytopenia, prevention; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT **Bone marrow**
 (transplant; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Chemotherapy
 Cytotoxic agents
 Immunoradiotherapy
 Lymphoma
 Tumor markers
 (treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT CD19 (antigen)
 Cytokines
 Interleukin 4
 Tumor necrosis factors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Antibodies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT CD20 (antigen)
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Radionuclides, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT Interferons
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (.alpha.; treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

IT 50-02-2, Dexamethasone 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 51-75-2, Mechlorethamine 53-03-2, Prednisone 57-22-7, Vincristine 147-94-4, Cytarabine 148-82-3, Melphalan 302-79-4, all-trans-Retinoic acid 671-16-9, Procarbazine 2068-78-2, Oncovin 3778-73-2, Ifosfamide 4291-63-8, Adenosine, 2-chloro-2'-deoxy- 4342-03-4, Dacarbazine 10043-66-0, Iodine-131, biological studies 10098-91-6, Yttrium-90, biological studies 11056-06-7, Bleomycin 15663-27-1, Cisplatin 15750-15-9, Indium-111, biological studies 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 33419-42-0, Etoposide 41575-94-4, Carboplatin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 65271-80-9, Mitozantrone 83869-56-1, GM-CSF 143011-72-7, G-CSF 174722-31-7, Rituximab
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of non-Hodgkins lymphoma with **bone marrow** involvement with anti-CD20 antibodies)

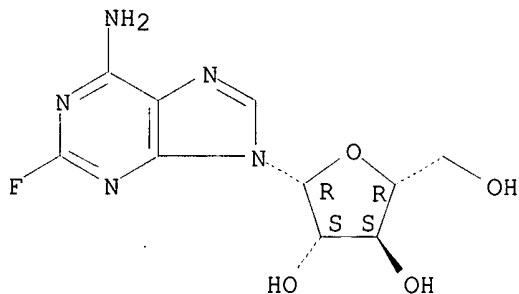
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Anderson; US 5843439 A 1998 HCAPLUS
- (2) Behr; Clin Can Res 1999, V5
- (3) Gopal; J Lab Clin Med 1999, V134 HCAPLUS
- (4) Kaminski; US 5595721 A 1997 HCAPLUS
- (5) Maloney; Oncology 1998, V12(8), P65
- (6) Wiseman; Clin Can Res 1999, V5 HCAPLUS
- (7) Witzig; J Clin Oncol 1999, V17(12) HCAPLUS

IT 21679-14-1, Fludarabine 143011-72-7, G-
 CSF
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of non-Hodgkins lymphoma with **bone marrow**
 involvement with anti-CD20 antibodies)
 RN 21679-14-1 HCAPLUS
 CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



RN 143011-72-7 HCAPLUS
 CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:475547 HCAPLUS
 DN 133:84250
 TI Use of adenosine agonists in cancer therapy for inducing
 proliferation of **hematopoietic** system cells
 IN Fishman, Pnina; Cohn, Ilan
 PA Can-Fite Technologies Ltd., Israel
 SO PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-70
 ICS C07H019-16
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 63
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000040251	A1	20000713	WO 2000-IL14	20000107 <--
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1140116	A1	20011010	EP 2000-900112	20000107 <--
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US 2001031742	A1	20011018	US 2001-782259	20010214 <--
US 2002037871	A1	20020328	US 2001-871963	20010604 <--

hematopoietic system cells)
 IT 36396-99-3 37739-05-2, 2-Chloro-N6-cyclopentyladenosine
 41552-82-3, N6-Cyclopentyladenosine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adenosine agonists in cancer therapy for inducing proliferation of hematopoietic system cells)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Glaxo Group Ltd; US 5998388 A HCAPLUS
- (2) Glaxo Group Ltd; WO 9743300 A 1997 HCAPLUS
- (3) Moos, W; JOURNAL OF MEDICINAL CHEMISTRY 1985, V28(10), P1383 HCAPLUS
- (4) Tey, H; BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 1992, V187(3), P1486 HCAPLUS
- (5) The United States Of America; US 5498605 A HCAPLUS
- (6) The United States Of America; WO 9402497 A 1994 HCAPLUS
- (7) Trivedi, B; US 4791103 A 1998 HCAPLUS
- (8) University Of Florida; US 5998387 A HCAPLUS
- (9) University Of Florida; WO 9724363 A 1997 HCAPLUS
- (10) Williams, M; DRUG DEVELOPMENT RESEARCH 1993, V28(3), P438 HCAPLUS

IT 36396-99-3 37739-05-2, 2-Chloro-N6-cyclopentyladenosine

41552-82-3, N6-Cyclopentyladenosine

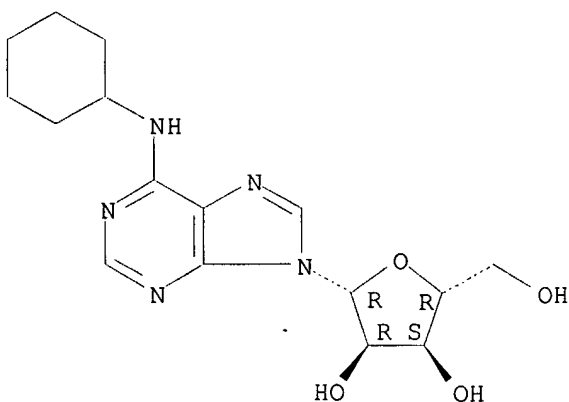
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adenosine agonists in cancer therapy for inducing proliferation of hematopoietic system cells)

RN 36396-99-3 HCAPLUS

CN Adenosine, N-cyclohexyl- (9CI) (CA INDEX NAME)

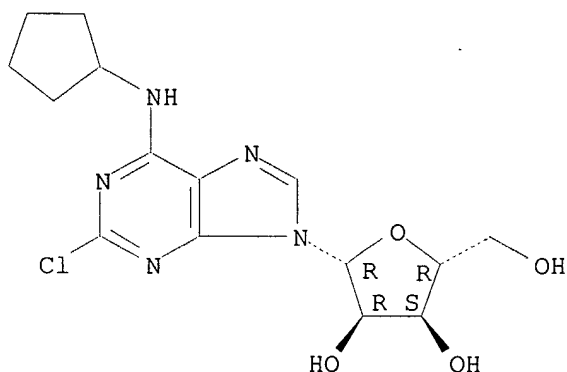
Absolute stereochemistry.



RN 37739-05-2 HCAPLUS

CN Adenosine, 2-chloro-N-cyclopentyl- (9CI) (CA INDEX NAME)

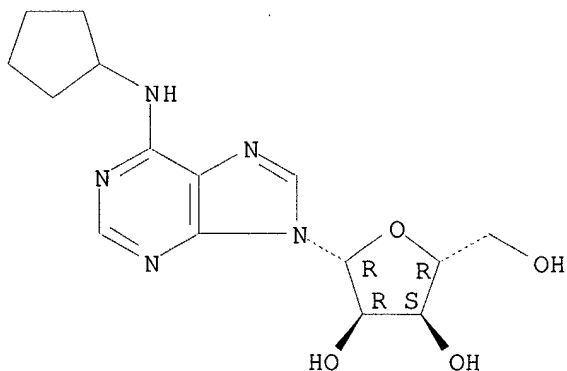
Absolute stereochemistry.



RN 41552-82-3 HCAPLUS

CN Adenosine, N-cyclopentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L174 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:291051 HCAPLUS

DN 133:26585

TI **Adenosine** acts as a chemoprotective agent by stimulating G-CSF production: a role for A1 and A3 **adenosine receptors**

AU **Fishman, Pnina**; Bar-Yehuda, Sara; Farbstein, Tamar; Barer, Faina; Ohana, Gil

CS Laboratory of Clinical and Tumor Immunology, The Felsenstein Medical Research Center, Rabin Medical Center, Tel-Aviv University, Petach-Tikva, Israel

SO Journal of Cellular Physiology (2000), 183(3), 393-398
CODEN: JCLLAX; ISSN: 0021-9541

PB Wiley-Liss, Inc.

DT Journal

LA English

CC 1-6 (Pharmacology)

Section cross-reference(s): 2

AB **Adenosine**, a ubiquitous nucleoside, is released into the extracellular environment from metabolically active or stressed cells. It binds to cells through specific A1, A2A, A2B, and A3 G-protein-assocd. cell-surface **receptors**, thus acting as a signal-transduction mol. by regulating the levels of adenylyl cyclase and phospholipase C. In this study, we showed that **adenosine** stimulates the proliferation of murine **bone marrow** cells in vitro. Pharmacol. studies, using antagonists to the **adenosine**

receptors, revealed that this activity was mediated through the binding of **adenosine** to its A1 and A3 **receptors**. This result was further corroborated by showing that the two selective A1 and A3 **receptor** agonists, N-cyclopentyladenosine (CPA) and 1-deoxy-1-[6-[[[3-iodophenyl)methyl]amino]-9H-purin-9-yl]-N-methyl-.beta.-D-ribofuranuronamide (**IB-MECA**) resp., induced **bone marrow** cell proliferation in a manner similar to **adenosine**. **Adenosine's** interaction with its A1 and A3 **receptors** induced G-CSF prodn., which led to its stimulatory effect on **bone marrow** cells. These results were confirmed in vivo when we demonstrated that low-dose **adenosine** (0.25 mg/kg) acted as a chemoprotective agent. When administered after chemotherapy, it restored the no. of leukocytes and neutrophils to normal levels, compared with the decline in these parameters after chemotherapy alone. It is suggested that low-dose **adenosine**, already in clin. use, may also be applied as a chemoprotective agent.

ST **adenosine** chemoprotectant CSF **receptor**

IT **Adenosine receptors**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(A1; **adenosine** acts as **bone**

marrow chemoprotective agent by stimulating **granulocyte**-CSF prodn. and role for **adenosine A1** and

A3 receptors therein)

IT **Adenosine receptors**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(A3; **adenosine** acts as **bone**

marrow chemoprotective agent by stimulating **granulocyte**-CSF prodn. and role for **adenosine A1** and

A3 receptors therein)

IT **Bone marrow**

Cytoprotective agents

Hematopoiesis

Leukocyte

Neutrophil

Signal transduction, biological

(**adenosine** acts as **bone marrow**

chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1** and **A3 receptors** therein)

IT 50-18-0, Cyclophosphamide

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(**adenosine** acts as **bone marrow**

chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1** and **A3 receptors** therein)

IT **41552-82-3, N-Cyclopentyladenosine 152918-18-8, IB-MECA**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**adenosine** acts as **bone marrow**

chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1** and **A3 receptors** therein)

IT 58-61-7, **Adenosine**, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**adenosine** acts as **bone marrow**

chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1** and **A3 receptors**

therein)
IT 143011-72-7, **Granulocyte-colony-stimulating factor**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(adenosine acts as bone marrow chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1 and A3 receptors** therein)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Bastin, B; Cell Immunol 1990, V128, P385 HCAPLUS
- (2) Belardinelli, L; Prog Cardiovasc Dis 1989, V32, P73 HCAPLUS
- (3) Bouma, M; J Immunol 1994, V153, P4159 HCAPLUS
- (4) Clarke, B; Int J Cardiol 1989, V23, P1 MEDLINE
- (5) Collis, M; Pharmacol Ther 1989, V41, P143 HCAPLUS
- (6) Cronstein, B; J Immunol 1992, V148, P2201 HCAPLUS
- (7) Derigs, H; Exp Hematol 1994, V22, P924 HCAPLUS
- (8) Djaldetti, M; Clin Exp Metastasis 1996, V14, P189 HCAPLUS
- (9) Dubey, R; Circulation 1997, V96, P2656 HCAPLUS
- (10) Epstein, J; Cancer Treat Rep 1984, V68, P1153 HCAPLUS
- (11) Fishman, P; Cancer Res 1998, V58, P3181 HCAPLUS
- (12) Gilbertsen, R; Agents Actions 1987, V22, P91 MEDLINE
- (13) Ikebuchi, K; Blood 1988, V72, P2007 HCAPLUS
- (14) Itoh, Y; Int J Hematol 1992, V55, P139 MEDLINE
- (15) Jackson, R; Br J Cancer 1978, V37, P701 HCAPLUS
- (16) Kitabayashi, A; Blood 1995, V86, P2220 HCAPLUS
- (17) Krishan, A; J Cell Biol 1975, V66, P188 MEDLINE
- (18) Kurland, J; Cancer Res 1977, V37, P4534 HCAPLUS
- (19) Lee, A; Blood 1999, V93, P537 HCAPLUS
- (20) Linden, J; FASEB J 1991, V5, P2668 HCAPLUS
- (21) Nagao, S; Cell Immunol 1984, V89, P427 HCAPLUS
- (22) Nilsson, J; Atherosclerosis 1984, V53, P77 HCAPLUS
- (23) Parmely, M; J Immunol 1993, V151, P389 HCAPLUS
- (24) Pastan, I; Annu Rev Biochem 1975, V44, P491 HCAPLUS
- (25) Patil, R; Blood 1995, V85, P80 HCAPLUS
- (26) Pospisil, M; Blood 1995, V86, P3692 HCAPLUS
- (27) Pospisil, M; Eur J Haematol 1998, V60, P172 HCAPLUS
- (28) Pospisil, M; Radiat Res 1993, V134, P323 HCAPLUS
- (29) Robson, R; Kidney Int 1995, V48, P1767 HCAPLUS
- (30) Soderback, U; Clin Sci 1991, V81, P691 MEDLINE
- (31) Stiles, G; Clin Res 1990, V38, P10 MEDLINE
- (32) Wagner, D; Circ Res 1998, V82, P47 HCAPLUS
- (33) Ward, A; Biochem Biophys Res Commun 1996, V224, P10 HCAPLUS
- (34) Wilson, N; Biochem Biophys Res Commun 1998, V244, P475 HCAPLUS

IT 41552-82-3, N-Cyclopentyladenosine 152918-18-8,
IB-MECA

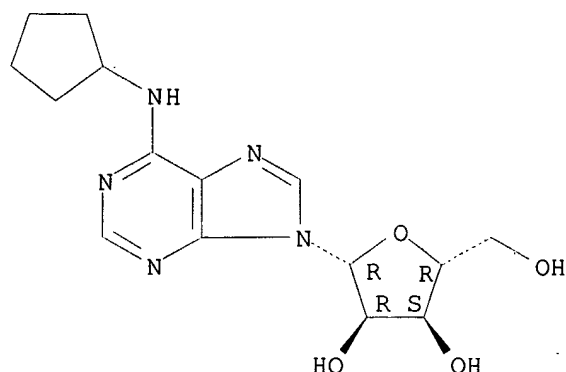
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(adenosine acts as bone marrow chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1 and A3 receptors** therein)

RN 41552-82-3 HCAPLUS

CN Adenosine, N-cyclopentyl- (9CI) (CA INDEX NAME)

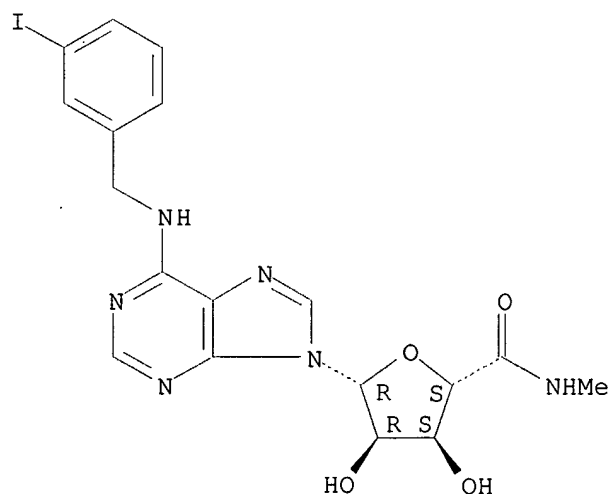
Absolute stereochemistry.



RN 152918-18-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-[6-[[(3-iodophenyl)methyl]amino]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 143011-72-7, **Granulocyte-colony-stimulating factor**

RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)

(adenosine acts as bone marrow

chemoprotective agent by stimulating **granulocyte-CSF** prodn. and role for **adenosine A1** and **A3 receptors** therein)

RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:261134 HCAPLUS

DN 133:53042

TI Clinically available drugs as potential curative means for treatment of radiation-induced **myelosuppression**

AU Hofer, M.; Pospisil, M.

CS Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno,

- 612 65, Czech Rep.
- SO NATO Science Series, 2: Environmental Security (1999),
55(Fundamentals for the Assessment of Risks from Environmental Radiation),
421-426
CODEN: NSESFA; ISSN: 1389-1839
- PB Kluwer Academic Publishers
- DT Journal; General Review
- LA English
- CC 1-0 (Pharmacology)
Section cross-reference(s): 8
- AB A review with 36 refs. The **bone marrow** syndrome
represents the most probable manifestation of the acute radiation disease
following medical application of ionizing radiation, as well as contingent
nuclear accidents. Protection and treatment of marrow damage induced by
radiation exposures in the range of sublethal and near LDs is, at present,
a serious medical problem. Moreover, radiation-induced hematopoietic
suppression may serve as a model for studying the effects of other
bone marrow damaging factors and medical procedures,
including cytostatic chemotherapy. Among the compds. tested as potential
stimulators of mammalian **hematopoiesis** damaged by ionizing
radiation in the Institute of Biophysics, Brno, Czech Republic, also clin.
available medicaments belonging to non-steroidal anti-inflammatory drugs
(NSAIDs) or drugs used in cardiovascular medicine were used. NSAIDs act
on the principle of inhibition of prostaglandin prodn. Prostaglandins
operate in neg. feedback control of **hematopoiesis**, esp.
granulopoiesis. Removal of this feedback enables to enhance prodn. of
functional blood cells. Indomethacin, diclofenac, flurbiprofen, and
nitroxybutylester of flurbiprofen have been successfully tested as
hematopoietic stimulators in irradiated mice. Administration of
flurbiprofen nitroxybutylester, a newly synthesized flurbiprofen deriv.,
appears to be esp. promising from the point of view of decreased
gastrointestinal toxicity of this compd. Dipyridamole (DP) and
adenosine monophosphate (AMP) used clin. for decreasing platelet
aggregation (DP) and as vasodilators and cardioprotectants (DP, AMP)
operate as enhancers of extracellular concn. of **adenosine**.
Receptor-based extracellular action of **adenosine** has
been found to stimulate **hematopoiesis** on the levels of stem and
progenitor cell populations. Interesting results on synergistic action of
DP + AMP and **granulocyte colony-stimulating**
factor (G-CSF) on mouse granulopoiesis have
been obtained as well. Haematopoiesis-enhancing effects of drugs
elevating extracellular **adenosine** may be of clin. importance
both from the point of view of medical benefit as well as from the
standpoint of contingent financial savings obtained when using these
unexpensive drugs.
- ST review radiation myelosuppression therapy **hematopoiesis**
- IT Cytoprotective agents
(cardioprotective; clin. available drugs as potential curative means
for treatment of radiation-induced myelosuppression)
- IT **Hematopoiesis**
Ionizing radiation
Nuclear reactor accident
Radioprotectants
Vasodilators
(clin. available drugs as potential curative means for treatment of
radiation-induced myelosuppression)
- IT **Hematopoiesis**
(disorders, myelosuppression; clin. available drugs as potential
curative means for treatment of radiation-induced myelosuppression)
- IT Anti-inflammatory agents
(nonsteroidal; clin. available drugs as potential curative means for
treatment of radiation-induced myelosuppression)
- RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bohacek, J; Life Sciences 1993, V53, P1317 HCAPLUS
- (2) Cronstein, B; J Immunol 1985, V135, P1366 HCAPLUS
- (3) Fedorocko, P; Immunopharmacol 1994, V28, P163 HCAPLUS
- (4) Floersheim, G; Radiat Res 1994, V139, P240 HCAPLUS
- (5) Fontagne, J; Exp Hematol 1980, V8, P1157 HCAPLUS
- (6) Gualtieri, R; Exp Hematol 1986, V14, P689 HCAPLUS
- (7) Hofer, M; Fol Biol (Praha) 1996, V42, P267 HCAPLUS
- (8) Hofer, M; J Leukoc Biol 1993, V53, P185 HCAPLUS
- (9) Hofer, M; Physiol Res 1992, V41, P157 HCAPLUS
- (10) Hofer, M; Physiol Res 1995, V44, P93 HCAPLUS
- (11) Hofer, M; Physiol Res 1996, V45, P213 HCAPLUS
- (12) Hofer, M; Physiol Res 1997, V46, P285 HCAPLUS
- (13) Hosek, B; Radiat Environm Biophys 1992, V31, P289 HCAPLUS
- (14) Juchelkova, L; Physiol Res 1998, V47, P73 HCAPLUS
- (15) Kozubik, A; Fol Biol (Praha) 1987, V33, P418 HCAPLUS
- (16) Kozubik, A; Fol Biol (Praha) 1990, V36, P291 MEDLINE
- (17) Kozubik, A; Int J Radiat Biol 1994, V65, P369 HCAPLUS
- (18) Kozubik, A; Strahlenther Onkol 1991, V167, P186 MEDLINE
- (19) Kozubik, A; Stud Biophys 1990, V131, P93
- (20) Kurland, J; Exp Hematol 1977, V5, P357 HCAPLUS
- (21) Nishiguchi, I; Radiat Res 1990, V122, P188 MEDLINE
- (22) Pelus, L; Immunol Res 1989, V8, P176 HCAPLUS
- (23) Pospisil, M; Acta Radiol Oncol 1986, V25, P195 HCAPLUS
- (24) Pospisil, M; Blood 1995, V86, P3692 HCAPLUS
- (25) Pospisil, M; Eur J Haematol 1998, V60, P172 HCAPLUS
- (26) Pospisil, M; Exp Hematol 1992, V20, P891 HCAPLUS
- (27) Pospisil, M; Experientia 1992, V48, P253 HCAPLUS
- (28) Pospisil, M; Physiol Res 1993, V42, P333 HCAPLUS
- (29) Pospisil, M; Radiat Res 1993, V134, P323 HCAPLUS
- (30) Pospisil, M; Radiat Res 1995, V142, P16 HCAPLUS
- (31) Pospisil, M; Strahlenther Onkol 1989, V165, P627 MEDLINE
- (32) Pospisil, M; Stud Biophys 1989, V132, P203 HCAPLUS
- (33) Rathbone, M; In Vitro Cell Developm Biol 1992, V28A, P529 HCAPLUS
- (34) Rathbone, M; Med Hypothes 1992, V37, P333
- (35) Serushago, B; Immunopharmacol 1987, V14, P21 HCAPLUS
- (36) Wallace, J; Gastroenterol 1994, V107, P173 HCAPLUS

L174 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:807344 HCAPLUS

DN 132:30462

TI Fludarabine, cytarabine, and **granulocyte-colony stimulating factor** for the treatment of high risk **myelodysplastic** syndromes

AU Ferrara, Felicetto; Leoni, Franco; Pinto, Antonio; Mirto, Salvatore; Morra, Enrica; Zagonel, Vittorina; Mele, Giuseppina; Ciolli, Stefania; Magrin, Silvana; Montillo, Marco

CS Divisione di Ematologia, Ospedale Cardarelli, Naples, 80128, Italy

SO Cancer (New York) (1999), 86(10), 2006-2013

CODEN: CANCAR; ISSN: 0008-543X

PB John Wiley & Sons, Inc.

DT Journal

LA English

CC 1-6 (Pharmacology)

AB BACKGROUND. The prognosis of patients with high risk myelodysplastic syndromes (MDS) (i.e., refractory anemia with excess of blasts [RAEB] and refractory anemia with excess of blasts in transformation [RAEB-t]) usually is poor. The combination of fludarabine, cytarabine, and **granulocyte-colony stimulating factor** (G-CSF) (FLAG regimen) has been reported to be effective in patients with these diseases. METHODS. Forty-two patients (32 with RAEB-t and 10 with RAEB) were treated with the FLAG regimen. The median age was 61 yr (range, 27-74 yr). Forty patients were diagnosed

with primary MDS and 2 patients had treatment-related MDS. Induction therapy was comprised of the FLAG regimen, whereas consolidation therapy included idarubicin and cytarabine. Patients with a compatible donor and who were age < 50 yr were scheduled to undergo an allogeneic **bone marrow** transplantation (BMT), whereas for those patients without a donor and who were age < 60 yr autologous BMT with peripheral blood stem cells mobilized by the consolidation regimen plus **G-CSF** was planned. RESULTS. Complete remission (CR) was achieved in 31 of 42 patients (74%; 95% confidence interval, 60-87%). Death during induction therapy occurred in 4 patients (9%) whereas 7 patients (17%) were resistant to the FLAG regimen. Toxicity from the consolidation regimen was negligible. All patients age < 50 yr and achieving CR were eligible for allogeneic BMT procedures, with early recurrence being the only reason for exclusion. The median overall survival and disease free survival were 13 mo and 18 mo, resp. Patients with favorable cytogenetics had a significantly better outcome compared with those patients with an adverse karyotype. CONCLUSIONS. The FLAG regimen is effective in patients with high risk MDS as well as in patients age > 60 yr. The toxicity of the regimen is low and the majority of patients are eligible to undergo allogeneic BMT procedures after induction/consolidation therapy.

ST fludarabine cytarabine G-CSF myelodysplastic syndrome antitumor
IT Transplant and Transplantation
Transplant and Transplantation
(**bone marrow**; fludarabine, cytarabine, and
G-CSF for treatment of high risk myelodysplastic
syndromes in humans)
IT Antitumor agents
Myelodysplastic syndromes
(fludarabine, cytarabine, and **G-CSF** for treatment
of high risk myelodysplastic syndromes in humans)
IT **Bone marrow**
Bone marrow
(transplant; fludarabine, cytarabine, and **G-CSF** for
treatment of high risk myelodysplastic syndromes in humans)
IT 147-94-4, Cytarabine 21679-14-1, Fludarabine 143011-72-7
, **Granulocyte-colony stimulating**
factor

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fludarabine, cytarabine, and **G-CSF** for treatment
of high risk myelodysplastic syndromes in humans)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Anderson, J; Blood 1993, V82, P677 MEDLINE
- (2) Anon; ISCN guidelines for cancer cytogenetics 1995
- (3) Bennett, J; Br J Haematol 1982, V51, P189 MEDLINE
- (4) Beran, M; Blood 1996, V90(Suppl 1), P583a
- (5) Bernstein, S; J Clin Oncol 1996, V14, P2486 MEDLINE
- (6) Buchner, T; Semin Oncol 1997, V24, P124 MEDLINE
- (7) Carella, A; Br J Haematol 1996, V95, P127 MEDLINE
- (8) De Witte, T; Blood 1996, V88(Suppl 1), P454a
- (9) De Witte, T; Blood 1997, V90, P3853 HCAPLUS
- (10) De Witte, T; Leukemia 1995, V9, P1805 MEDLINE
- (11) Estey, E; Blood 1997, V90, P2969 HCAPLUS
- (12) Estey, E; J Clin Oncol 1994, V12, P671 MEDLINE
- (13) Estey, E; Leukemia 1996, V10(Suppl 2), P39
- (14) Fenaux, P; Br J Haematol 1991, V77, P497 MEDLINE
- (15) Ferrara, F; Blood 1997, V90(Suppl 1), P85a
- (16) Ferrara, F; Leuk Lymphoma 1998, P375 MEDLINE
- (17) Ferrara, F; Leuk Res 1997, V21(Suppl 1), P48a
- (18) Fleischack, G; Br J Haematol 1998, V102, P647
- (19) Gallagher, A; Haematologica 1997, V82, P191 HCAPLUS

- (20) Gandhi, V; J Clin Oncol 1993, V11, P116 MEDLINE
- (21) Gassmann, W; Semin Hematol 1996, V33, P196 MEDLINE
- (22) Greenberg, P; Blood 1998, V89, P2079
- (23) Hofmann, W; Semin Hematol 1996, V33, P177 MEDLINE
- (24) Invernizzi, R; Haematologica 1997, V82, P660 HCAPLUS
- (25) Kaplan, E; J Am Stat Assoc 1958, V53, P457
- (26) Kouides, P; Semin Hematol 1996, V33, P95 MEDLINE
- (27) List, A; J Clin Oncol 1990, V8, P1424 MEDLINE
- (28) Lowenthal, R; Int J Hematol 1997, V65, P319 MEDLINE
- (29) Michelutti, A; Haematologica 1997, V82, P143 HCAPLUS
- (30) Montillo, M; Am J Hematol 1998, V58, P105 HCAPLUS
- (31) Nokes, T; Leuk Lymphoma 1997, V27, P93 MEDLINE
- (32) Parker, J; Br J Haematol 1997, V99, P939 HCAPLUS
- (33) Ruutu, T; Leuk Res 1997, V21, P133 HCAPLUS
- (34) Sanz, G; Leuk Res 1992, V16, P77 MEDLINE
- (35) Tafuri, A; Leukemia 1990, V4, P826 MEDLINE
- (36) Terpstra, W; Leukemia 1997, V11, P315 HCAPLUS
- (37) To Boerkhost, P; Leukemia 1994, V8, P1480
- (38) Van der Lely, N; Ann Hematol 1994, V68, P225 MEDLINE
- (39) Verbeek, W; Ann Hematol 1997, V74, P205 HCAPLUS
- (40) Wattel, E; Br J Haematol 1997, V98, P983 MEDLINE

IT 21679-14-1, Fludarabine 143011-72-7, **Granulocyte**

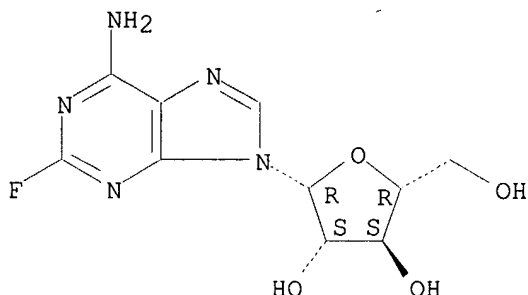
-colony stimulating factor

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fludarabine, cytarabine, and **G-CSF** for treatment of high risk myelodysplastic syndromes in humans)

RN 21679-14-1 HCAPLUS

CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:631898 HCAPLUS

DN 131:237646

TI Topotecan and cytarabine is an active combination regimen in **myelodysplastic** syndromes and chronic **myelomonocytic leukemia**

AU Beran, Miloslav; Estey, Elihu; O'Brien, Susan; Cortes, Jorge; Koller, Charles A.; Giles, Francis J.; Kornblau, Steven; Andreeff, Michael; Vey, Norbert; Pierce, Sherry R.; Hayes, Kimberly; Wong, Gee Chuan; Keating, Michael; Kantarjian, Hagop

CS Departments of Leukemia and Molecular Hematology, and Division of

Laboratory Medicine, The University of Texas M.D. Anderson Cancer Center,
Houston, TX, 77030, USA

SO Journal of Clinical Oncology (1999), 17(9), 2819-2830
CODEN: JCONDN; ISSN: 0732-183X

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 1-6 (Pharmacology)

AB The aim of this study was to evaluate the efficacy and safety of the combination of topotecan and cytarabine in patients with myelodysplastic syndromes (MDSs) and chronic myelomonocytic leukemia (CMML). Fifty-nine patients with MDSs and 27 with CMML were enrolled. They were either previously untreated (66%) or had received only biol. agents (14%) or chemotherapy with or without biol. agents (20%). Treatment consisted of topotecan 1.25 mg/m² by continuous i.v. infusion daily for 5 days and cytarabine 1.0 g/m² by infusion over 2 h daily for 5 days. Prophylaxis included antibacterial, antifungal, and antiviral agents. At a median follow-up of 7 mo, all 86 patients were assessable for response and toxicity. Complete remission (CR) was obsd. in 48 patients (56%; 61% with MDSs, 44% with CMML; $P = .15$). Similar CR rates were obsd. for patients with good-risk and poor-risk MDS (70% and 56%, resp.). The treatment effectively induced CR in patients with a poor-prognosis karyotype involving chromosomes 5 and 7 (CR, 71%) and secondary MDSs (CR, 72%). Fifty-four patients received one induction course, 25 patients received two, and the rest received more than two. The median no. of continuation courses was two. The median overall duration of CR was 34 wk (50 wk for MDSs and 33 wk for CMML). The median survival was 60 wk for MDS and 44 wk for CMML patients. CR and survival durations were longer in patients with refractory anemia with excess blasts (RAEB). Grade 3 or 4 mucositis or diarrhea was obsd. in three patients each. Fever was obsd. in 63%, and infections in 49% of patients. Six patients (7%) died during induction therapy. Topotecan and cytarabine induced high CR rates in unselected patients with MDSs and CMML, particularly among patients with poor-prognosis cytogenetics and secondary MDSs. Topotecan-cytarabine is an active induction regimen in MDS and CMML patients, is well tolerated, and is assocd. with a low mortality rate.

ST topotecan cytarabine myelodysplastic syndrome myelomonocytic leukemia

IT Toxicity

(drug; effect of topotecan and cytarabine in myelodysplastic syndromes and chronic myelomonocytic leukemia)

IT **Myelodysplastic syndromes**

(effect of topotecan and cytarabine in myelodysplastic syndromes and chronic myelomonocytic leukemia)

IT Antitumor agents

(myelomonocytic leukemia; effect of topotecan and cytarabine in myelodysplastic syndromes and chronic myelomonocytic leukemia)

IT 147-94-4, Cytarabine 302-79-4, Trans-Retinoic acid 21679-14-1, Fludarabine 58957-92-9, Idarubicin 123948-87-8, Topotecan 143011-72-7, GCSF

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of topotecan and cytarabine in myelodysplastic syndromes and chronic myelomonocytic leukemia)

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD

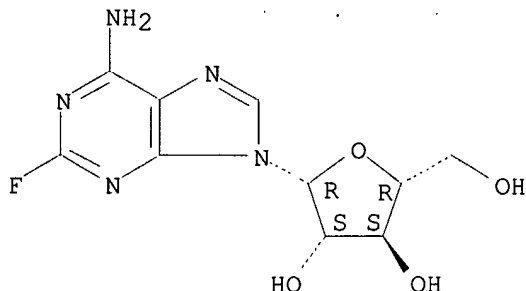
RE

- (1) Armitage, J; Cancer Treat Rep 1981, V65, P601 MEDLINE
- (2) Aul, C; Br J Haematol 1992, V82, P358 MEDLINE
- (3) Aul, C; Leukemia 1994, V8, P1906 MEDLINE
- (4) Bennett, J; Br J Haematol 1982, V51, P189 MEDLINE
- (5) Bennett, J; Br J Haematol 1994, V87, P746 MEDLINE
- (6) Bennett, J; Clin Haematol 1986, V15, P909 MEDLINE
- (7) Beran, M; Blood 1996, V88, P2473 HCAPLUS

- (8) Beran, M; Leuk Lymphoma 1998, V31, P521 MEDLINE
 - (9) Beran, M; Myelodysplastic Syndromes Pathophysiology and Treatment 1988, P155
 - (10) Bernstein, S; J Clin Oncol 1996, V14, P2486 MEDLINE
 - (11) Cambier, N; Hematol Cell Ther 1997, V39, P41 MEDLINE
 - (12) Cheson, B; J Clin Oncol 1986, V4, P1857 MEDLINE
 - (13) Coiffier, B; Cancer 1987, V60, P3029 MEDLINE
 - (14) Cooper, B; J Clin Oncol 1996, V15, P486
 - (15) Crump, M; Blood 1996, V88, P867
 - (16) Dewitte, T; Leukemia 1995, V9, P1805 MEDLINE
 - (17) Economopoulos, T; Leuk Lymphoma 1996, V20, P385 HCAPLUS
 - (18) Estey, E; Blood 1995, V90, P2843
 - (19) Estey, E; Blood 1997, V90, P2969 HCAPLUS
 - (20) Estey, E; Blood 1997, V90, P416
 - (21) Estey, E; Blood 1999, V93, P2478 HCAPLUS
 - (22) Estey, E; Cytokines Mol Ther 1995, V1, P21 MEDLINE
 - (23) Estey, E; J Clin Oncol 1994, V12, P671 MEDLINE
 - (24) Estey, E; Leuk Lymphoma 1993, V11, P59
 - (25) Fenaux, P; Br J Haematol 1991, V77, P497 MEDLINE
 - (26) Fenaux, P; J Clin Oncol 1988, V6, P1417 MEDLINE
 - (27) Ghaddar, H; Leukemia 1994, V8, P1269 MEDLINE
 - (28) Greenberg, P; Blood 1993, V82, P196
 - (29) Greenberg, P; Blood 1997, V89, P2079 HCAPLUS
 - (30) Hellstrom-Lindberg, E; Br J Haematol 1995, V89, P67 MEDLINE
 - (31) Hochsler, H; Camptothecins:New Anticancer Agents 1995, P93
 - (32) Hsiang, Y; Cancer Res 1988, V48, P1722 HCAPLUS
 - (33) Hsiang, Y; Cancer Res 1989, V49, P5077 HCAPLUS
 - (34) Invernizzi, R; Haematologica 1997, V82, P9 HCAPLUS
 - (35) Jacobs, R; Blood 1986, V67, P1765 MEDLINE
 - (36) Kantarjian, H; Blood 1993, V81, P1146 MEDLINE
 - (37) Kantarjian, H; Cancer 1986, V58, P2023 MEDLINE
 - (38) Kantarjian, H; Hematology/Oncology Clinics of North America 1990, V4, P389 MEDLINE
 - (39) Keating, M; Cancer 1982, V50, P457 MEDLINE
 - (40) Kerkhofs, H; Br J Haematol 1987, V65, P73 MEDLINE
 - (41) Martiat, P; Blood 1991, V78, P205 MEDLINE
 - (42) Mertelsmann, R; Blood 1980, V56, P733
 - (43) Michaux, J; Leuk Lymphoma 1993, V9, P35 MEDLINE
 - (44) Miller, K; Ann Hematol 1993, V66, P164
 - (45) Morel, P; Leukemia 1993, V7, P1315 MEDLINE
 - (46) Mufti, G; Br J Haematol 1985, V59, P425 MEDLINE
 - (47) National Cancer Institute; Guidelines for Reporting of Adverse Drug Reactions Bethesda 1988
 - (48) Parker, J; Br J Haematol 1997, V99, P939 HCAPLUS
 - (49) Preisler, H; N Engl J Med 1983, V308, P21 MEDLINE
 - (50) Rowinsky, E; Clin Cancer Res 1996, V2, P1921 HCAPLUS
 - (51) Rowinsky, E; J Clin Oncol 1994, V12, P2193 MEDLINE
 - (52) Rowinsky, E; Semin Oncol 1997, V24(suppl 20), PS20
 - (53) Ruutu, T; Leuk Res 1997, V21, P133 HCAPLUS
 - (54) Sanz, G; Blood 1989, V74, P395 MEDLINE
 - (55) Schuster, M; J Clin Oncol 1990, V9, P205
 - (56) Seiter, K; J Clin Oncol 1997, V15, P44 HCAPLUS
 - (57) Vallespi, T; Br J Haematol 1985, V61, P83 MEDLINE
 - (58) Verweig, J; Camptothecins:New Anticancer Agents 1995, P105
 - (59) Wattel, E; Br J Haematol 1997, V98, P983 MEDLINE
 - (60) Zhang, H; Cancer Cells 1990, V2, P23 HCAPLUS
- IT 21679-14-1, Fludarabine 143011-72-7, GCSF
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effect of topotecan and cytarabine in myelodysplastic syndromes and chronic myelomonocytic leukemia)
- RN 21679-14-1 HCAPLUS

CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:427884 HCAPLUS

DN 131:97038

TI Fludarabine-containing regimens severely impair peripheral blood stem cells mobilization and collection in acute **myeloid leukemia** patients

AU Visani, G.; Lemoli, R. M.; Tosi, P.; Martinelli, G.; Testoni, N.; Ricci, P.; Piccaluga, P. P.; Pastano, R.; Leopardi, G.; Dizdari, A.; Motta, M. R.; Rizzi, S.; Tura, S.

CS Institute of Haematology and Medical Oncology 'L. e A. Seragnoli', University of Bologna, Bologna, 40138, Italy

SO British Journal of Haematology (1999), 105(3), 775-779
CODEN: BJHEAL; ISSN: 0007-1048

PB Blackwell Science Ltd.

DT Journal

LA English

CC 1-6 (Pharmacology)

AB We studied the effects of an intensified induction/consolidation treatment contg. fludarabine (ICE/FLAN/FLAN) on the mobilization and collection of peripheral blood stem cells (PBSC) in 31 consecutive untreated acute myeloid leukemia (AML) patients. The complete remission (CR) rate was comparable to classic inductions (68% after ICE: 84% after ICE-FLAN I). To mobilize PBSC, 19 patients received 10 .mu.g/kg/d of **granulocyte-colony stimulating factor (G-CSF)** starting at day 13 after FLAN, 13 (69%) of whom were found to be nonmobilizers. When a second **G-CSF** administration was performed in 10/13 patients mobilization was either not achieved (8/10) or was considered insufficient (<1.times.10⁶ CD34+ cells/kg) (2/10) and all 13 were subsequently submitted to **bone marrow** harvest. The harvest was considered adequate in 12/13 (92%) patients and autologous BMT (ABMT) has so far been performed in 10/12 cases with a mean of 8.6.times.10⁸/kg nucleated reinfused cells. The median times to neutrophil and platelet recovery after ABMT did not significantly differ from those of two previous series of patients treated with ABMT without fludarabine-contg. regimens. Adequate amts. of PBSC were obtained in 6/19 (31%) patients, who were then reinfused. Median times for platelet recovery were significantly longer than in a previous series of 26 AML cases reinfused with PBSC after treatment with the ICE-NOVIA induction/consolidation regimen (125 v 20d to 20.times.10⁹ plt/l, P < 0.02: 218 v 37d to

50.times.109 plt/l, $P < 0.02$). In addn., times for platelet recovery after ICE/FLAN/FLAN were not significantly different from those in a previous group treated with ABMT performed after ICE/NOVIA, without fludarabine. We conclude that fludarabine-contg. regimens severely impair mobilization and collection of PBSC in AML patients and seem unsuitable when PBSC autotransplantation is programmed.

ST fludarabine stem cell mobilization myeloid leukemia

IT Antitumor agents

(acute myelogenous leukemia; fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

IT Transplant and Transplantation

(autotransplant, peripheral blood stem cell; fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

IT Hematopoietic precursor cell

(stem; fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

IT 21679-14-1, Fludarabine

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

IT 143011-72-7, Granulocyte-colony stimulating factor

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bennett, J; British Journal of Haematology 1977, V33, P451
- (2) Burnett, A; Lancet 1998, V351, P700 HCAPLUS
- (3) Cheson, B; Journal of Clinical Oncology 1990, V8, P813 MEDLINE
- (4) Clavio, M; Haematologica 1996, V81, P513 HCAPLUS
- (5) Demirer, T; Bone Marrow Transplantation 1996, V18, P29 MEDLINE
- (6) Estey, E; Journal of Clinical Oncology 1994, V12, P671 MEDLINE
- (7) Gorin, N; Annals of Oncology 1995, V4(Suppl 1), P59
- (8) Johnson, S; Lancet 1996, V347, P1432 HCAPLUS
- (9) Korbling, M; Bone Marrow Transplantation 1991, V7, P343 MEDLINE
- (10) Laporte, J; Lancet 1997, Vii, P1993
- (11) Lemoli, R; Blood 1996, V87, P1625 HCAPLUS
- (12) Lemoli, R; to be published in Bone Marrow Transplantation 1999
- (13) Lowenberg, B; Journal of Clinical Oncology 1997, V8, P287
- (14) Martin, C; Bone Marrow Transplantation 1998, V21, P375 MEDLINE
- (15) Mehta, J; Bone Marrow Transplantation 1995, V15, P652 MEDLINE
- (16) Miggiano, M; Leukemia 1996, V10, P402 MEDLINE
- (17) Montillo, M; Leukemia and Lymphoma 1994, V15, P187 MEDLINE
- (18) Motta, R; Experimental Hematology 1997, V25, P1261
- (19) Reiffers, J; International Journal of Cell Cloning 1992, V7(Suppl 1), P111
- (20) Sanz, M; Journal of Clinical Oncology 1993, V11, P1661 MEDLINE
- (21) Schiller, G; Leukemia 1997, V11, P1533 MEDLINE
- (22) Schlenk, R; British Journal of Haematology 1997, V99, P386 MEDLINE
- (23) Sorensen, J; Journal of Clinical Oncology 1997, V15, P458 HCAPLUS
- (24) Testoni, N; Bone Marrow Transplantation 1998, V22, P1065 MEDLINE
- (25) To, L; Bone Marrow Transplantation 1992, V9, P277 MEDLINE
- (26) Visani, G; Cryobiology 1990, V27, P103 MEDLINE
- (27) Visani, G; Leukemia 1994, V8, P1842 MEDLINE

IT 21679-14-1, Fludarabine

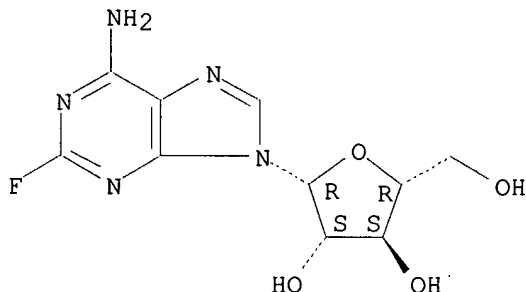
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

RN 21679-14-1 HCAPLUS

CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 143011-72-7, **Granulocyte-colony**

stimulating factor

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fludarabine-contg. regimens severely impair peripheral blood stem cell mobilization and collection in humans with acute myeloid leukemia)

RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:245744 HCAPLUS

DN 130:346997

TI **Randomized phase II study of fludarabine + cytosine arabinoside + idarubicin .+-. all-trans retinoic acid .+-. granulocyte colony-stimulating factor in poor prognosis newly diagnosed acute myeloid leukemia and myelodysplastic syndrome**

AU Estey, Elihu H.; Thall, Peter F.; Pierce, Sherry; Cortes, Jorge; Beran, Miloslav; Kantarjian, Hagop; Keating, Michael J.; Andreeff, Michael; Freireich, Emil

CS Department of Leukemia, Division of Medicine, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA

SO Blood (1999), 93(8), 2478-2484

CODEN: BLOOAW; ISSN: 0006-4971

PB W. B. Saunders Co.

DT Journal

LA English

CC 1-6 (Pharmacology)

Section cross-reference(s): 15, 18

AB Preclin. data suggest that retinoids, eg, all-trans retinoic acid (ATRA), lower concns. of antiapoptotic proteins such as bcl-2, possibly thereby improving the outcome of anti-acute myeloid leukemia (AML) chemotherapy.

Granulocyte colony-stimulating factor

(G-CSF) has been considered to be potentially synergistic with ATRA in this regard. Accordingly, we randomized 215 patients with newly diagnosed AML (153 patients) or high-risk myelodysplastic syndrome (MDS) (refractory anemia with excess blasts [RAEB] or RAEB-t, 62 patients) to receive fludarabine + ara-C + idarubicin (FAI) alone, FAI + ATRA, FAI + G-CSF, or FAI + ATRA + G-CSF. Eligibility required one of the following: age over 71 yr, a history of abnormal blood counts before M.D. Anderson (MDA)

presentation, secondary AML/MDS, failure to respond to one prior course of chemotherapy given outside MDA, or abnormal renal or hepatic function. For the two treatment arms contg. ATRA, ATRA was given 2 days (day-2) before beginning and continued for 3 days after completion of FAI. For the two treatment arms including G-CSF, G-CSF began on day-1 and continued until neutrophil recovery. Patients with white blood cell (WBC) counts >50,000/.mu.L began ATRA on day 1 and G-CSF on day 2. Events (death, failure to achieve complete remission [CR], or relapse from CR) have occurred in 77% of the 215 patients. Reflecting the poor prognosis of the patients entered, the CR rate was only 51%, median event-free survival (EFS) time once in CR was 36 wk, and median survival time was 28 wk. A Cox regression anal. indicated that, after accounting for patient prognostic variables, none of the three adjuvant treatment combinations (FAI + ATRA, FAI + G, FAI + ATRA + G) affected survival, EFS, or EFS once in CR compared with FAI. Similarly, there were no significant effects of either ATRA ignoring G-CSF, or of G-CSF ignoring ATRA. As previously found, a diagnosis of RAEB or RAEB-t rather than AML was insignificant. There were no indications that the effect of ATRA differed according to cytogenetic group, diagnosis (AML or MDS), or treatment schedule. Logistic regression anal. indicated that, after accounting for prognosis, addn. of G-CSF +/- ATRA to FAI improved CR rate vs. either FAI or FAI + ATRA, but G-CSF had no effect on the other outcomes. We conclude that addn. of ATRA +/- G-CSF to FAI had no effect on CR rate, survival, EFS, or EFS in CR in poor prognosis, newly diagnosed AML or high-risk MDS.

ST fludarabine cytosine arabinoside idarubicin retinoate colony stimulating factor leukemia

IT Antitumor agents

(myelogenous leukemia; randomized phase II study of fludarabine + cytosine arabinoside + idarubicin +/- all-trans retinoic acid +/- **granulocyte colony-stimulating factor** in poor prognosis newly diagnosed human acute myeloid leukemia and myelodysplastic syndrome)

IT **Myelodysplastic syndromes**

(randomized phase II study of fludarabine + cytosine arabinoside + idarubicin +/- all-trans retinoic acid +/- **granulocyte colony-stimulating factor** in poor prognosis newly diagnosed human acute myeloid leukemia and myelodysplastic syndrome)

IT 147-94-4, Cytosine arabinoside 302-79-4, Retinoic acid
21679-14-1, Fludarabine 58957-92-9, Idarubicin
143011-72-7, **Granulocyte colony-stimulating factor**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(randomized phase II study of fludarabine + cytosine arabinoside + idarubicin +/- all-trans retinoic acid +/- **granulocyte colony-stimulating factor** in poor prognosis newly diagnosed human acute myeloid leukemia and myelodysplastic syndrome)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Banker, D; Blood 1997, V89, P243 HCAPLUS
- (2) Becker, R; The New S Language 1988
- (3) Campos, L; Blood 1993, V81, P3091 MEDLINE
- (4) Cleveland, W; J Am Stat Assoc 1979, V74, P829
- (5) Cox, D; J R Stat Soc B 1972, V34, P187
- (6) Dombret, H; N Engl J Med 1995, V332, P1678 MEDLINE
- (7) Estey, E; Blood 1997, V90, P2969 HCAPLUS
- (8) Estey, E; Blood 1997, V90(suppl 1, abstr), P416a

- (9) Estey, E; J Clin Oncol 1994, V12, P671 MEDLINE
- (10) Fenaux, P; Leuk Lymphoma 1995, V16, P431 MEDLINE
- (11) Fisher, R; J R Stat Soc 1924, V87, P442
- (12) Fleming, T; Counting Processes and Survival Analysis 1991
- (13) Godwin, J; Blood 1998, V91, P3607 HCAPLUS
- (14) Grambsch, P; Biometrika 1994, V81, P515
- (15) Heil, G; Blood 1997, V90, P4710 HCAPLUS
- (16) Hoffman-La Roche, Inc; Tretinoin package insert 1995
- (17) Hu, Z; Leukemia 1995, V9, P1667 MEDLINE
- (18) Hu, Z; Leukemia 1996, V10, P1925 MEDLINE
- (19) Hu, Z; Leukemia 1996, V10, P410 MEDLINE
- (20) Kaplan, E; J Am Stat Assoc 1958, V53, P457
- (21) Lishner, M; Leukemia 1989, V3, P784 MEDLINE
- (22) Mantel, N; Cancer Chemother Rep 1966, V60, P163
- (23) Maung, Z; Br J Haematol 1994, V88, P105 MEDLINE
- (24) Mehta, C; Stat Methods Med Res 1994, V3, P135 MEDLINE
- (25) Minn, A; Blood 1995, V86, P1903 HCAPLUS
- (26) Pocock, S; Biometrics 1975, V31, P103 MEDLINE
- (27) Ravandi-Kashani, F; Blood 1995, V86(suppl 1, abstr), P776a
- (28) Snedecor, G; Statistical Methods, (ed 7) 1980
- (29) Tallman, M; N Engl J Med 1997, V337, P1021 MEDLINE
- (30) Therneau, T; A package for survival analysis 1994
- (31) Yang, G; Leukemia 1994, V8, P2065 MEDLINE

IT 21679-14-1, Fludarabine 143011-72-7, **Granulocyte colony-stimulating factor**

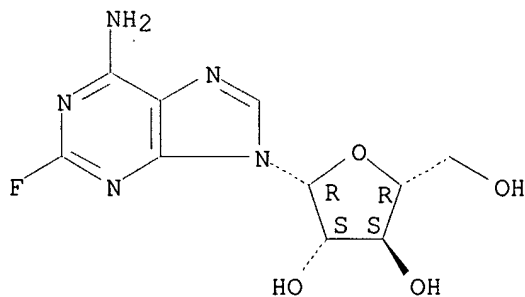
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(randomized phase II study of fludarabine + cytosine arabinoside + idarubicin .+-. all-trans retinoic acid .+-. **granulocyte colony-stimulating factor** in poor prognosis newly diagnosed human acute myeloid leukemia and myelodysplastic syndrome)

RN 21679-14-1 HCAPLUS

CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:64673 HCAPLUS

DN 130:90536

TI Adenosine and active agents interacting with the adenosine system as **adjunctive** therapeutic agents

IN Cohn, Ilan; Fishman, Pnina

PA **Can-Fite Technologies Ltd., Israel**
 SO PCT Int. Appl., 40 pp.
 CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC **1-12** (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902143	A2	19990121	WO 1998-IL324	19980710 <--
	WO 9902143	A3	19990812		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IL 121272	A1	20000601	IL 1997-121272	19970710 <--
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	EP 994702	A2	20000426	EP 1998-932488	19980710 <--
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	JP 2001509479	T2	20010724	JP 2000-501739	19980710 <--
PRAI	IL 1997-121272	A	19970710 <--		
	WO 1998-IL324	W	19980710 <--		
AB	Adenosine and active agent which interact with the adenosine system are used to treat conditions of weakened, immune system, as an anti-cancer therapy and for improving the therapeutic index of a variety of therapeutic drugs.				
ST	adenosine adjunctive therapeutic agent immune system cancer therapy				
IT	Adenosine receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (A1; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)				
IT	Adenosine receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (A2; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)				
IT	Mammary gland Mammary gland Mammary gland (adenocarcinoma, inhibitors; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)				
IT	Antipsychotics Antitumor agents Chemotherapy Drug delivery systems Drug interactions Drugs Immunostimulants Leukocyte Leukocytopenia Lymphocyte Monocyte Mononuclear cell (leukocyte) Polymorphonuclear leukocyte Tranquilizers				

(adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Interleukin 12
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Nucleosides, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (and nucleoside derivs.; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Cell proliferation
 (bone marrow cell; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Prostate gland
 (carcinoma, inhibitors; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Bone marrow
 (cell, proliferation; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Toxicity
 (drug; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Antitumor agents
 Antitumor agents
 (erythroleukemia; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Antitumor agents
 (lymphoma; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Antitumor agents
 Antitumor agents
 Antitumor agents
 (mammary gland adenocarcinoma; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Antitumor agents
 (melanoma; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Antitumor agents
 (myelogenous leukemia; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Lymphocyte
 (natural killer cell; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT Antitumor agents
 (prostate carcinoma; adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT 50-18-0, Cyclophosphamide
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT 58-61-7, Adenosine, biological studies
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (adenosine and active agents interacting with the adenosine system as adjunctive therapeutic agents)

IT 58-55-9, Theophylline, biological studies 102146-07-6, DPCPX
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)
 (adenosine and active agents interacting with the adenosine system as
 adjunctive therapeutic agents)

- L174 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2002 ACS
 AN 1998:576814 HCAPLUS
 DN 129:170044
 TI Gene transfer into **hematopoietic** stem cells and clinical
 application of the technique
 AU Ozawa, Keiya
 CS Dep. Hematol., Jichi Med. Sch., Tochigi, 329-04, Japan
 SO Nippon Naika Gakkai Zasshi (1998), 87(8), 1526-1531
 CODEN: NNGAAS; ISSN: 0021-5384
 PB Nippon Naika Gakkai
 DT Journal; General Review
 LA Japanese
 CC 1-0 (Pharmacology)
 Section cross-reference(s): 3
 AB A review with 5 refs., on (1) vectors, methods, and efficacy of gene
 transfer into hematopoietic stem cells (HSC), (2) current status of clin.
 application of HSC-targeted gene therapy for **adenosine** deaminase
 deficiency and other diseases, and (3) development of selective amplifier
 genes. A chimeric gene encoding the fusion protein between the
granulocyte colony-stimulating factor
receptor and the hormone-binding domain of estrogen
receptor is discussed.
 ST review gene therapy hematopoietic stem cell; transfer gene hematopoietic
 stem cell review
 IT Gene therapy
 Transformation, genetic
 (current status of hematopoietic stem cell-targeted gene therapy)
 IT Gene, animal
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); THU (Therapeutic use);
 BIOL (Biological study); PROC (Process); USES (Uses)
 (current status of hematopoietic stem cell-targeted gene therapy)
 IT **Hematopoietic precursor cell**
 (stem; current status of hematopoietic stem cell-targeted gene therapy)
- L174 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2002 ACS
 AN 1998:476930 HCAPLUS
 DN 129:254464
 TI Evaluation of **marrow** and blood hemopoietic progenitors in
 chronic lymphocytic **leukemia** before and after chemotherapy
 AU Sala, Roberta; Mauro, Francesca R.; Bellucci, Roberto; De Propriis, Maria
 Stefania; Cordone, Iole; Lisci, Alessandro; Foa, Robin; De Fabritiis,
 Paolo
 CS Department of Cellular Biotechnology and Haematology, University "La
 Sapienza", Rome, Italy
 SO European Journal of Haematology (1998), 61(1), 14-20
 CODEN: EJHAEC; ISSN: 0902-4441
 PB Munksgaard International Publishers Ltd.
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 AB We have evaluated the no. and differentiation pattern of CD34+ cells, as
 well as the CFU-GM, BFU-E and CFU-GEMM progenitors from the blood (PB) and
 marrow (BM) of 53 chronic lymphocytic leukemia (CLL) patients.
 Twenty-four patients were untreated and 29 were studied at 2 mo from the
 last course of fludarabine or chlorambucil; 6 patients, studied after
 fludarabine therapy, were further evaluated after mobilization with
 cyclophosphamide and **G-CSF**. PB of untreated patients
 showed a median no. of CD34+ cells, CFU-GM, BFU-E and CFU-GEMM/105 seeded

cells and per L of PB similar to those of normal controls. No differences were also found in the no. of clonogenic progenitors/105 cells in patients studied before and after therapy, while significantly fewer BFU-E/1 of PB were found after fludarabine. The no. of circulating CD34+ cells/l of PB was significantly lower in patients treated with fludarabine or chlorambucil compared to untreated patients. BM growth was significantly reduced in untreated CLL patients compared to healthy donors. Treatment with fludarabine or chlorambucil restored BM progenitors at levels similar to those of normal controls; this effect did not occur for CFU-GM in patients treated with fludarabine. Three-color fluorescence anal. demonstrated a differentiation pattern of CD34+ cells, with a greater expression of CD13 and CD33 after treatment with fludarabine compared to untreated patients and normal controls. In 4 patients previously treated with fludarabine who underwent a successful cyclophosphamide and G-CSF mobilization therapy, 4.times.106 CD34+ cells/kg were collected. These 4 patients showed a notable increase of CD34+ cells and of clonogenic cells in the PB, but a marked decrease of BM progenitor cells. The 2 patients who failed CD34+ cell mobilization had a reduced CFU-GM growth both in the PB and in the BM. Taken together, these studies indicate that residual hemopoietic progenitors are present in untreated CLL patients and that stem cell mobilization and collection can be carried out following fludarabine treatment.

ST chlorambucil fludarabine cyclophosphamide GCSF antileukemic

IT Antitumor agents

(leukemia; evaluation of marrow and blood hemopoietic progenitors in chronic lymphocytic leukemia before and after chemotherapy in humans)

IT 50-18-0, Cyclophosphamide 305-03-3, Chlorambucil 21679-14-1, Fludarabine 143011-72-7, G-CSF

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(evaluation of marrow and blood hemopoietic progenitors in chronic lymphocytic leukemia before and after chemotherapy in humans)

IT 21679-14-1, Fludarabine 143011-72-7, G-CSF

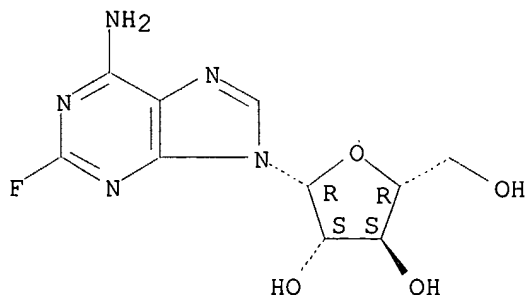
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(evaluation of marrow and blood hemopoietic progenitors in chronic lymphocytic leukemia before and after chemotherapy in humans)

RN 21679-14-1 HCAPLUS

CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:240962 HCAPLUS

DN 129:22933

TI **Granulocyte colony-stimulating**

factor and drugs elevating extracellular adenosine synergize to enhance **hematopoietic** reconstitution in irradiated mice

AU Pospisil, M.; Hofer, M.; Znojil, V.; Netikova, J.; Vacha, J.; Hola, J.; Vacek, A.

CS Institute Biophysics, Academy Sciences Czech Republic, Brno, Czech Rep.

SO European Journal of Haematology (1998), 60(3), 172-180

CODEN: EJHAEC; ISSN: 0902-4441

PB Munksgaard International Publishers Ltd.

DT Journal

LA English

CC 1-4 (Pharmacology)

AB The activation of **adenosine receptors** has recently been demonstrated to stimulate **hematopoiesis**. In the present study, we investigated the ability of drugs elevating extracellular **adenosine** to influence curative effects of **granulocyte colony-stimulating factor** (G-CSF) in mice exposed to a sublethal dose of 4 Gy of ⁶⁰Co radiation. Elevation of extracellular **adenosine** in mice was induced by the combined administration of dipyridamole, a drug inhibiting the cellular uptake of **adenosine**, and **adenosine** monophosphate (AMP), an **adenosine** prodrug. The effects of dipyridamole plus AMP, and G-CSF, administered either alone or in combination, were evaluated. The drugs were injected to mice in a 4-d treatment regimen starting on d 3 after irradiation and the hematopoietic response was evaluated on d 7, 10, 14, 18 and 24 after irradiation. While the effects of G-CSF on the late maturation stages of blood cells, appearing shortly after the completion of the treatment, were not influenced by dipyridamole plus AMP, positive effects of the combination therapy occurred in the post-irradiation recovery phase which is dependent on the repopulation of hematopoietic stem cells. This was indicated by the significant elevation of counts of granulocyte-macrophage progenitor cells (GM-CFC) and granulocytic cells in the **bone marrow** (d 14), of GM-CFC (d 14), granulocytic and erythroid cells (d 14 and 18) in spleen, and of neutrophils (d 18), monocytes (d 14 and 18) and platelets (d 18) in the peripheral blood. These effects suggest that the repopulation potential of the combination therapy lies in a common multilineage cell population. The results of this study implicate the promising possibility to enhance the curative effects of G-CSF under conditions of myelosuppressive states induced by radiation exposure.

ST **granulocyte colony stimulating factor** adenosine **hematopoiesis**; irradiation **hematopoiesis** GCSF AMP

IT **Hematopoiesis**

Polymorphonuclear leukocyte

(**granulocyte colony-stimulating**

factor and drugs elevating extracellular adenosine synergize to enhance hematopoietic reconstitution in irradiated mice)

IT **Adenosine receptors**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**granulocyte colony-stimulating**

factor and drugs elevating extracellular **adenosine** synergize to enhance hematopoietic reconstitution in irradiated mice)

IT **Hematopoietic precursor cell**

(granulocyte-macrophage; **granulocyte colony-**

stimulating factor and drugs elevating extracellular **adenosine** synergize to enhance hematopoietic reconstitution in

irradiated mice)
IT Gamma ray
(irradn.; **granulocyte colony-stimulating factor** and drugs elevating extracellular adenosine synergize to enhance hematopoietic reconstitution in irradiated mice)
IT Drug interactions
(synergistic; **granulocyte colony-stimulating factor** and drugs elevating extracellular adenosine synergize to enhance hematopoietic reconstitution in irradiated mice)
IT 58-32-2, Dipyridamole 61-19-8, Amp, biological studies
143011-72-7, Granulocyte colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**granulocyte colony-stimulating factor** and drugs elevating extracellular adenosine synergize to enhance hematopoietic reconstitution in irradiated mice)
IT 58-61-7, Adenosine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**granulocyte colony-stimulating factor** and drugs elevating extracellular adenosine synergize to enhance hematopoietic reconstitution in irradiated mice)
IT **143011-72-7, Granulocyte colony-stimulating factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**granulocyte colony-stimulating factor** and drugs elevating extracellular adenosine synergize to enhance hematopoietic reconstitution in irradiated mice)
RN 143011-72-7 HCAPLUS
CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

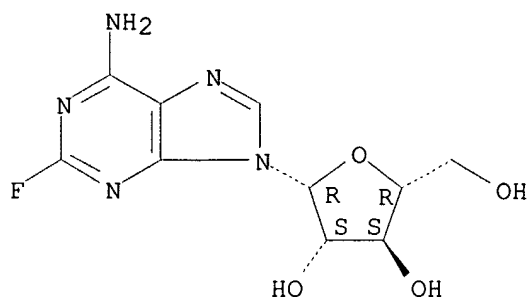
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:749200 HCAPLUS
DN 128:70450
TI Fludarabine and **granulocyte colony-stimulating factor (G-CSF)** in patients with chronic lymphocytic leukemia
AU O'Brien, S.; Kantarjian, H.; Beran, M.; Koller, C.; Talpaz, M.; Lerner, S.; Keating, M. J.
CS Department of Hematology, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SO Leukemia (1997), 11(10), 1631-1635
CODEN: LEUKED; ISSN: 0887-6924
PB Stockton Press
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 2
AB The study was designed to det. whether administration of **granulocyte colony-stimulating factor (G-CSF)** following fludarabine would reduce the incidences of myelosuppression and infections. Twenty-five previously treated patients with Rai stage III-IV chronic lymphocytic leukemia (CLL) received fludarabine 30 mg/m² daily for 5 days each month. **G-CSF** was given at 5 .mu.g/kg s.c. starting 1 day after chemotherapy (day 6) and continued until the next course unless the granulocyte count was .gtoreq.10 000/.mu.l. The incidences of myelosuppression and infection were compared with those seen in an historical control

population of 145 previously treated patients with Rai stage III-IV CLL who were given the same schedule of fludarabine without growth factor. There was a significant decrease in myelosuppression; patients receiving **G-CSF** developed neutropenia at a neutrophil count $<1000/\mu\text{l}$ or $500/\mu\text{l}$ in 45% and 15% of courses vs 79% ($P = 0.002$) and 63% ($P < 0.001$) of historical controls. Twenty percent of **G-CSF**-treated patients had therapy delayed by >35 days per course, vs 50% of historical controls ($P = 0.005$). The incidence of pneumonia was 8% with **G-CSF** and 37% without in historical controls. Other infection rates (sepsis, fever of undetd. origin, minor infections) were similar. This decrease in pneumonia was noted even in high-risk groups such as patients older than 60 yr and patients with hypogammaglobulinemia. The use of **G-CSF** following fludarabine in high-risk patients with CLL resulted in a significant decrease in myelosuppression and pneumonia. Larger trials to verify these results and to compare costs are indicated.

- ST GCSF fludarabine myelosuppression chronic lymphocytic leukemia
 IT Fever and Hyperthermia
 Immunostimulants
 Pneumonia
 Sepsis
 (G-CSF to prevent fludarabine-induced
 myelosuppression in humans with chronic lymphocytic leukemia)
 IT **Leukemia**
 (chronic lymphocytic; G-CSF to prevent
 fludarabine-induced myelosuppression in humans with chronic lymphocytic
 leukemia)
 IT **Hematopoiesis**
 (disorders, myelosuppression; G-CSF to prevent
 fludarabine-induced myelosuppression in humans with chronic lymphocytic
 leukemia)
 IT **21679-14-1, Fludarabine**
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (G-CSF to prevent fludarabine-induced
 myelosuppression in humans with chronic lymphocytic leukemia)
 IT **143011-72-7, G-CSF**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (G-CSF to prevent fludarabine-induced
 myelosuppression in humans with chronic lymphocytic leukemia)
 IT **21679-14-1, Fludarabine**
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (G-CSF to prevent fludarabine-induced
 myelosuppression in humans with chronic lymphocytic leukemia)
 RN 21679-14-1 HCAPLUS
 CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



IT 143011-72-7, G-CSF

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G-CSF to prevent fludarabine-induced myelosuppression in humans with chronic lymphocytic leukemia)

RN 143011-72-7 HCAPLUS

CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L174 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:79794 HCAPLUS

DN 126:166179

TI Poor-risk acute **myelogenous leukemia** patients undergoing the fludarabine-cytosine arabinoside - filgrastim regimen: multidrug resistance expression, **granulocyte colony-stimulating factor** priming activity and clinical response

AU Petti, M. C.; Martelli, M. P.; Tosti, S.; De Felice, L.; Valentini, T.; Tafuri, A.; Petrucci, M. T.; Mandelli, F.

CS Department of Hematology, University La Sapienza, Rome, Italy

SO Haematology and Blood Transfusion (1997), 38(Acute Leukemias VI), 846-851

CODEN: HBTRDV; ISSN: 0171-7111

PB Springer

DT Journal

LA English

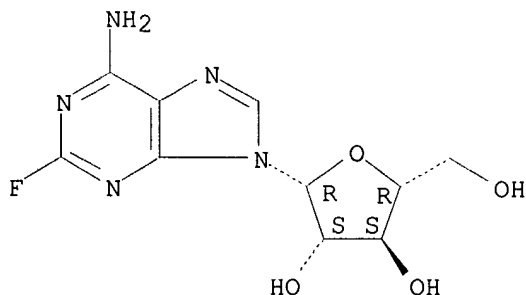
CC 1-6 (Pharmacology)

AB Eleven poor-risk acute myelogenous leukemia (AML) patients were treated with fludarabine + cytosine arabinoside + **granulocyte colony-stimulating factor** (FLAG). The median age was 38 (range 31-51 yr) and five patients were female. Six patients were resistant to a previous induction chemotherapy (European Organization for Research on Treatment of Cancer, EORTC, AML10 protocol), two patients had AML secondary to myelodysplastic syndrome, one had chronic myelomonocytic leukemia and two patients were in first resistant or subsequent relapse. According to the French-American-British (FAB) classification, patients presented with the following subtypes: four M4/M5, three not classifiable, two M2, one CMML, one M6. Seven patients achieved a complete remission (CR) (63%), of these four patients were MDR pos. The median time to achieve CR was 39.5 days (range 28-49 days). Four patients relapsed after 1, 2, 3, 3 mo, resp., while three patients (all MDR pos.) are still in CR after 3, 7, and 12 mo. In the authors' experience, no major toxicities were obsd. during the treatment, except mild mucositis. The authors' results confirm the feasibility of this schedule and its efficacy in poor-risk AML, suggesting a preferential role in AML patients expressing the MDR phenotype.

ST fludarabine cytosine arabinoside filgrastim multidrug resistance;

- multidrug resistance granulocyte factor leukemia antitumor
- IT **Leukemia**
(acute myelogenous; poor-risk acute myelogenous leukemia human patients undergoing fludarabine-cytosine arabinoside - filgrastim regimen dealing with multidrug resistance expression, **granulocyte colony-stimulating factor** priming activity and clin. response)
- IT Antitumor agents
Multidrug resistance
(poor-risk acute myelogenous leukemia human patients undergoing fludarabine-cytosine arabinoside - filgrastim regimen dealing with multidrug resistance expression, **granulocyte colony-stimulating factor** priming activity and clin. response)
- IT 71-30-7, Cytosine **21679-14-1**, Fludarabine 50986-18-0, Arabinoside 121181-53-1, Filgrastim **143011-72-7**, Colony-stimulating factor, granulocyte
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(poor-risk acute myelogenous leukemia human patients undergoing fludarabine-cytosine arabinoside - filgrastim regimen dealing with multidrug resistance expression, **granulocyte colony-stimulating factor** priming activity and clin. response)
- IT **21679-14-1**, Fludarabine **143011-72-7**, Colony-stimulating factor, granulocyte
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(poor-risk acute myelogenous leukemia human patients undergoing fludarabine-cytosine arabinoside - filgrastim regimen dealing with multidrug resistance expression, **granulocyte colony-stimulating factor** priming activity and clin. response)
- RN 21679-14-1 HCAPLUS
CN 9H-Purin-6-amine, 9-.beta.-D-arabinofuranosyl-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 143011-72-7 HCAPLUS
CN Colony-stimulating factor, granulocyte (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> fil reg

FILE 'REGISTRY' ENTERED AT 07:41:18 ON 22 OCT 2002

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DICTIONARY FILE UPDATES: 20 OCT 2002 HIGHEST RN 463296-69-7

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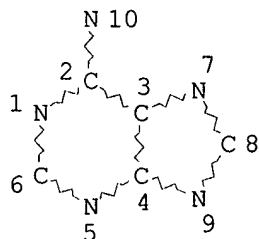
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Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L54 STR



NODE ATTRIBUTES:

NSPEC IS RC AT 10
CONNECT IS M1 RC AT 1
CONNECT IS M1 RC AT 6
CONNECT IS M1 RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 1
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.02

56975 ANSWERS

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SUBSTANCE IDENTIFICATION.

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L217 ANSWER 1 OF 5 MEDLINE
AN 2000224990 MEDLINE
DN 20224990 PubMed ID: 10763920
TI Oral administration of muscle derived small molecules inhibits tumor spread while promoting normal cell growth in mice.
AU Bar-Yehuda S; Farbstein T; Barer F; Ohana G; **Fishman P**
CS Laboratory of Clinical and Tumor Immunology, The Felsenstein Medical Research Center, Tel-Aviv University, Rabin Medical Center, Petach-Tikva, Israel.
SO CLINICAL AND EXPERIMENTAL METASTASIS, (1999) 17 (6) 531-5.
Journal code: 8409970. ISSN: 0262-0898.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000427
AB Tumor metastases are extremely rare in striated muscles. This is surprising given the fact that this tissue constitutes 60% of body weight. The present study focuses on small molecules produced and secreted by muscle cells which possess anti-cancer activity in vivo. Recently we have shown that a low molecular weight fraction (< 1000 Dalton) of skeletal muscle cell conditioned medium (muscle factor-MF), markedly inhibits the proliferation of carcinoma, sarcoma or melanoma cell lines in vitro. The MF exerts a cytostatic effect on tumor cell growth and arrests the cells in the G0/G1 of the cell cycle. However, normal cell proliferation, such as bone marrow and fibroblasts, was stimulated following incubation with MF. In this study, the effect of orally administered MF on melanoma and sarcoma growth was examined in mice. The administration of MF to mice inoculated intravenously with melanoma (B16-F10) or sarcoma (MCA-105) cells, resulted in a statistically significant inhibition of metastatic lung foci. In a different model, melanoma was induced in the foot pad and after development of a local lesion, the leg was amputated. A prolonged survival time was observed in the MF treated groups. Since the MF stimulated bone marrow cell proliferation in vitro, we decided to test its efficacy as an inhibitor of the myelotoxic effect exerted by chemotherapy, in vivo. MF, administered after chemotherapy, restored the number of white blood cells and yielded an increased percentage of neutrophils compared with the decline in these parameters after administration of chemotherapy alone. Thus, it is indicated that MF exerted a systemic anti tumor and chemoprotective effect when given orally. It can be concluded that it is bioavailable and is not biodegradable in the digestive system. MF may be considered as a potential therapy for the prevention of tumor spread.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Administration, Oral
Antineoplastic Agents: AE, adverse effects
Bone Marrow Cells: DE, drug effects
Bone Marrow Cells: PA, pathology
Cell Division: DE, drug effects
Cell Line
Lung Neoplasms: DT, drug therapy
*Lung Neoplasms: PC, prevention & control
*Lung Neoplasms: SC, secondary
Mice

Mice, Inbred C57BL

*Muscle Proteins: AD, administration & dosage

Muscle Proteins: PD, pharmacology

Sarcoma, Experimental: DT, drug therapy

*Sarcoma, Experimental: PA, pathology

CN 0 (Antineoplastic Agents); 0 (Muscle Proteins)

L217 ANSWER 2 OF 5 MEDLINE

AN 199397465 MEDLINE

DN 99397465 PubMed ID: 10470864

TI **Granulocyte colony-stimulating**

factor and drugs elevating extracellular adenosine act additively to enhance the hemopoietic spleen colony formation in irradiated mice.

AU Hofer M; Pospisil M; Netikova J; Znojil V; Vacha J

CS Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno.

SO PHYSIOLOGICAL RESEARCH, (1999) 48 (1) 37-42.

Journal code: 9112413. ISSN: 0862-8408.

CY Czech Republic

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199910

ED Entered STN: 19991014

Last Updated on STN: 19991014

Entered Medline: 19991007

AB The effects of combined administration of two drugs elevating extracellular adenosine, namely dipyridamole (DP) and adenosine monophosphate (AMP), and **granulocyte colony-**

stimulating factor (G-CSF) on hemopoietic stem cells in vivo were investigated. The experiments were performed on mice using the endogenous spleen colony formation in gamma-irradiated animals as an endpoint. The results have shown that DP and AMP act additively with **G-CSF** to enhance spleen colony formation and thus the erythroid repopulation of the spleen. These findings indicate that the signaling pathways of **G-CSF** and drugs elevating extracellular adenosine can interact at the level of primitive hemopoietic stem cells. The enhancement of hemopoiesis-stimulating effects of **G-CSF** by DP and AMP, which are low-priced and clinically available drugs, could improve the cost-effectiveness of the therapy with **G-CSF**.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't

*Adenosine: ME, metabolism

Adenosine Monophosphate: PD, pharmacology

Cell Count

Cobalt Radioisotopes

Colony-Forming Units Assay

Dipyridamole: PD, pharmacology

Erythroid Progenitor Cells: CY, cytology

*Extracellular Space: ME, metabolism

Gamma Rays

*Granulocyte Colony-Stimulating Factor: PD, pharmacology

*Hematopoiesis: DE, drug effects

Hematopoietic Stem Cells: CY, cytology

Mice

*Spleen: CY, cytology

*Whole-Body Irradiation

RN 143011-72-7 (Granulocyte Colony-Stimulating Factor); 58-32-2

(Dipyridamole); 58-61-7 (Adenosine); 61-19-8 (Adenosine

Monophosphate)

CN 0 (Cobalt Radioisotopes)

L217 ANSWER 3 OF 5 MEDLINE

AN 1998343581 MEDLINE

DN 98343581 PubMed ID: 9679987
TI Adenosine and other low molecular weight factors released by muscle cells inhibit tumor cell growth.
AU Fishman P; Bar-Yehuda S; Vagman L
CS Laboratory of Clinical and Tumor Immunology, The Felsenstein Medical Research Center, Tel-Aviv University, Rabin Medical Center, Petach-Tikva, Israel.. pfishma@ibm.net
SO CANCER RESEARCH, (1998 Jul 15) 58 (14) 3181-7.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980820
Last Updated on STN: 19980820
Entered Medline: 19980807
AB In this study, we investigated the basis of the resistance of muscles to tumor metastases. We found that a low molecular weight fraction (Mr <3000) of skeletal muscle cell-conditioned medium (MCM) markedly inhibits the proliferation of carcinoma, sarcoma, or melanoma cell lines in vitro. The MCM exerts a cytostatic effect on tumor cell growth and arrests the cells in G0/G1 of the cell cycle. However, normal cell proliferation of cells such as bone marrow cells or fibroblasts was found to be refractory to the influence of the MCM. A reduction in melanoma growth was observed in mice treated with the MCM. Adenosine was identified as one of the active components in the MCM by using high-performance liquid chromatography separations, mass spectra, and nuclear magnetic resonance analyses. At a concentration of 4 microM, equal to that found in the MCM, adenosine inhibits the proliferation of tumor cell lines (Nb2 lymphoma, K-562 leukemia, and LNCaP prostate carcinoma cells) while stimulating the proliferation of normal murine bone marrow cells. By similar methods, additional inhibitory components were detected in the MCM in a molecular mass range of 600-800 Da. The ability of adenosine and other low molecular weight components to specifically inhibit tumor cell growth in vitro and in vivo may account for the resistance of muscle to tumor metastases.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Adenosine: PD, pharmacology
Cell Cycle: DE, drug effects
*Cell Division: DE, drug effects
*Culture Media, Conditioned: PD, pharmacology
Mice
*Muscles: CH, chemistry
*Neoplasms: PC, prevention & control
Rats
Tumor Cells, Cultured: DE, drug effects
RN 58-61-7 (Adenosine)
CN 0 (Culture Media, Conditioned)
L217 ANSWER 4 OF 5 MEDLINE
AN 1998208194 MEDLINE
DN 98208194 PubMed ID: 9548416
TI Granulocyte colony-stimulating factor and drugs elevating extracellular adenosine synergize to enhance haematopoietic reconstitution in irradiated mice.
AU Pospisil M; Hofer M; Znojil V; Netikova J; Vacha J; Hola J; Vacek A
CS Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno.
SO EUROPEAN JOURNAL OF HAEMATOLOGY, (1998 Mar) 60 (3) 172-80.
Journal code: 8703985. ISSN: 0902-4441.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 199804
ED Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980428
AB The activation of **adenosine receptors** has recently been demonstrated to stimulate haematopoiesis. In the present study, we investigated the ability of drugs elevating extracellular **adenosine** to influence curative effects of **granulocyte colony-stimulating factor** (G-CSF) in mice exposed to a sublethal dose of 4 Gy of ⁶⁰Co radiation. Elevation of extracellular **adenosine** in mice was induced by the combined administration of dipyridamole, a drug inhibiting the cellular uptake of **adenosine**, and **adenosine** monophosphate (AMP), an **adenosine** prodrug. The effects of dipyridamole plus AMP, and G-CSF, administered either alone or in combination, were evaluated. The drugs were injected to mice in a 4-d treatment regimen starting on d 3 after irradiation and the haematopoietic response was evaluated on d 7, 10, 14, 18 and 24 after irradiation. While the effects of G-CSF on the late maturation stages of blood cells, appearing shortly after the completion of the treatment, were not influenced by dipyridamole plus AMP, positive effects of the combination therapy occurred in the post-irradiation recovery phase which is dependent on the repopulation of haematopoietic stem cells. This was indicated by the significant elevation of counts of granulocyte-macrophage progenitor cells (GM-CFC) and granulocytic cells in the bone marrow (d 14), of GM-CFC (d 14), granulocytic and erythroid cells (d 14 and 18) in the spleen, and of neutrophils (d 18), monocytes (d 14 and 18) and platelets (d 18) in the peripheral blood. These effects suggest that the repopulation potential of the combination therapy lies in a common multilineage cell population. The results of this study implicate the promising possibility to enhance the curative effects of G-CSF under conditions of myelosuppressive states induced by radiation exposure.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
*Adenosine: ME, metabolism
*Adenosine Monophosphate: PD, pharmacology
Blood Platelets: DE, drug effects
Dipyridamole: PD, pharmacology
Drug Synergism
*Erythrocytes: DE, drug effects
*Granulocyte Colony-Stimulating Factor: PD, pharmacology
Granulocyte-Macrophage Colony-Stimulating Factor: DE, drug effects
Granulocyte-Macrophage Colony-Stimulating Factor: RE, radiation effects
*Granulocytes: DE, drug effects
Granulocytes: RE, radiation effects
*Hematopoietic Stem Cells: DE, drug effects
Hematopoietic Stem Cells: RE, radiation effects
Lymphocytes: DE, drug effects
Mice
Mice, Inbred BALB C
Mice, Inbred CBA
Monocytes: DE, drug effects
Platelet Aggregation Inhibitors: PD, pharmacology
Receptors, Purinergic P1: ME, metabolism
RN 143011-72-7 (Granulocyte Colony-Stimulating Factor); 58-32-2 (Dipyridamole); 58-61-7 (Adenosine); 61-19-8 (Adenosine Monophosphate); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
CN 0 (Platelet Aggregation Inhibitors); 0 (Receptors, Purinergic P1)
L217 ANSWER 5 OF 5 MEDLINE
AN 96068733 MEDLINE
DN 96068733 PubMed ID: 7579335

TI Synergistic effect of **granulocyte colony-stimulating factor** and drugs elevating extracellular adenosine on neutrophil production in mice.
 AU Pospisil M; Hofer M; Znojil V; Vacha J; Netikova J; Hola J
 CS Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno, Czech Republic.
 SO BLOOD, (1995 Nov 15) 86 (10) 3692-7.
 Journal code: 7603509. ISSN: 0006-4971.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199512
 ED Entered STN: 19960124
 Last Updated on STN: 19960124
 Entered Medline: 19951219
 AB Experimental evidence suggests that the activation of purinoceptors by extracellular adenosine can modulate proliferation and/or differentiation of hematopoietic cells. The present study was undertaken to investigate the potential interactions of this system of intercellular signaling with the effects of **granulocyte colony-stimulating factor (G-CSF)** on granulopoiesis in vivo. Elevation of extracellular adenosine in normal mice was induced by the joined administration of dipyridamole, a drug inhibiting the cellular uptake of adenosine, and adenosine monophosphate (AMP), an adenosine prodrug. The effects of dipyridamole, AMP, and **G-CSF**, administered either alone or in combinations, were evaluated. The agents were injected to mice in a 4-day regimen, and the hematologic endpoints were determined 24 hours after the completion of the treatment. It was shown that the effects of **G-CSF**, ie, increases in peripheral blood neutrophils, granulocyte-macrophage progenitor cells (GM-CFC), and morphologically determined granulocytic cells in femoral marrow and a decrease in the marrow erythroid cells, can be enhanced by the combination of dipyridamole plus AMP administered 30 minutes before **G-CSF**. Furthermore, it was ascertained that the stimulatory action of dipyridamole plus AMP was expressed particularly at lower doses of **G-CSF** (1.5, 3, and 4.5 micrograms/d). At higher doses of **G-CSF** (6 and 9 micrograms/d), the interactions were no more evident. When combining dipyridamole, AMP, and 3 micrograms of **G-CSF**, peripheral neutrophils increased approximately 3.9- to 4.5-fold compared with an approximate 2.2-fold increase induced by **G-CSF** alone. The results indicate the possible therapeutic potential of combination therapy with **G-CSF** and drugs increasing extracellular adenosine.
 CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
 *Adenosine: BI, biosynthesis
 *Adenosine Monophosphate: PD, pharmacology
 Cell Differentiation: DE, drug effects
 Cell Division: DE, drug effects
 *Dipyridamole: PD, pharmacology
 Drug Synergism
 *Extracellular Space: ME, metabolism
 Filgrastim
 *Granulocyte Colony-Stimulating Factor: PD, pharmacology
 *Hematopoiesis: DE, drug effects
 *Hematopoietic Stem Cells: DE, drug effects
 Mice
 Mice, Inbred C57BL
 Mice, Inbred CBA
 *Neutrophils: CY, cytology
 Recombinant Proteins: PD, pharmacology
 RN 121181-53-1 (Filgrastim); 143011-72-7 (**Granulocyte Colony-Stimulating Factor**); 58-32-2 (Dipyridamole); 58-61-7 (Adenosine);

61-19-8 (Adenosine Monophosphate)
CN 0 (Recombinant Proteins)

=> d his

(FILE 'HOME' ENTERED AT 06:53:55 ON 22 OCT 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 06:55:37 ON 22 OCT 2002

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L1      1 S 143011-72-7
L2      4 S 163042-96-4 OR 152918-27-9 OR 152918-18-8 OR 89705-21-5
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L3 (      86)SEA FILE=HCAPLUS ABB=ON PLU=ON ("FISHMAN P"/AU OR "FISHMAN P
L4 (      7)SEA FILE=HCAPLUS ABB=ON PLU=ON ("CAN FITE BIOPHARMA LTD"/PA O
L5 (     88)SEA FILE=HCAPLUS ABB=ON PLU=ON (L3 OR L4)
L6 (     34)SEA FILE=HCAPLUS ABB=ON PLU=ON AB MECA
L7 (    139)SEA FILE=HCAPLUS ABB=ON PLU=ON IB MECA
L8 (     40)SEA FILE=HCAPLUS ABB=ON PLU=ON CL IB MECA
L9 (    341)SEA FILE=HCAPLUS ABB=ON PLU=ON "ADENOSINE RECEPTORS (L) A3"/C
L10 (   707)SEA FILE=HCAPLUS ABB=ON PLU=ON ADENOSIN?(L)A3(L)RECEPTOR
L11 (   261)SEA FILE=HCAPLUS ABB=ON PLU=ON ("RECEPTORS (L) PURINERGIC P1"
L12 (   280)SEA FILE=HCAPLUS ABB=ON PLU=ON "ADENOSINE RECEPTORS"/CT(L)AGO
L13 (  4518)SEA FILE=HCAPLUS ABB=ON PLU=ON ADENOSIN?(L)RECEPTOR(L)AGONIST
L14 (   429)SEA FILE=HCAPLUS ABB=ON PLU=ON ADENOSIN?(L)RECEPTOR(L)AGONIST
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L16 (     4)SEA FILE=REGISTRY ABB=ON PLU=ON 89705-21-5 OR 152918-27-9 OR
L17 (     1)SEA FILE=REGISTRY ABB=ON PLU=ON 120-73-0
L18 (     1)SEA FILE=REGISTRY ABB=ON PLU=ON 58-61-7
L19 (   138)SEA FILE=HCAPLUS ABB=ON PLU=ON L16
L20 (    25)SEA FILE=HCAPLUS ABB=ON PLU=ON 2 CHLORO N6 3 IODOBENZYL ADENO
L21 (    48)SEA FILE=HCAPLUS ABB=ON PLU=ON N6 3 IODOBENZYL ADENOSINE 5 N
L22 (     9)SEA FILE=HCAPLUS ABB=ON PLU=ON N6 2 4 AMINOPHENYL ETHYL ADENO
L23 (     5)SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND (L19 OR L20 OR L21 OR L
L24 (    15)SEA FILE=HCAPLUS ABB=ON PLU=ON (L15 OR L23)
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L26 (    12)SEA FILE=HCAPLUS ABB=ON PLU=ON CI IB MECA
L27 (    56)SEA FILE=HCAPLUS ABB=ON PLU=ON A3AR
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L32 (   100)SEA FILE=REGISTRY ABB=ON PLU=ON L31 AND 333.446/RID
L33 (    96)SEA FILE=REGISTRY ABB=ON PLU=ON L32 NOT L16
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L41 (   96506)SEA FILE=REGISTRY SSS FUL L40
L42      STR
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L44 (     3)SEA FILE=REGISTRY ABB=ON PLU=ON L39 AND CAMP
L45 (    95)SEA FILE=REGISTRY ABB=ON PLU=ON L39 NOT L44
L46 (    94)SEA FILE=REGISTRY ABB=ON PLU=ON L45 NOT 58-55-9
L47 (    93)SEA FILE=REGISTRY ABB=ON PLU=ON L46 NOT 118-00-3
L48 (    84)SEA FILE=REGISTRY ABB=ON PLU=ON L47 NOT GUANOS?
L49 (    47)SEA FILE=REGISTRY ABB=ON PLU=ON L48 AND L43
L50 (    37)SEA FILE=REGISTRY ABB=ON PLU=ON L48 NOT L49
L51 (    19)SEA FILE=REGISTRY ABB=ON PLU=ON L41 AND L50

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L55      56975 SEA FILE=REGISTRY SUB=L53 CSS FUL L54
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L56 ( 181680)SEA FILE=REGISTRY ABB=ON  PLU=ON  333.446/RID
L57      STR
L58 ( 56975)SEA FILE=REGISTRY SUB=L56 CSS FUL L57
L59      STR
L60      107 SEA FILE=REGISTRY SUB=L58 CSS FUL L59
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L61 ( 181680)SEA FILE=REGISTRY ABB=ON  PLU=ON  333.446/RID
L62      STR
L63 ( 56975)SEA FILE=REGISTRY SUB=L61 CSS FUL L62
L64      STR
L65 ( 47535)SEA FILE=REGISTRY SUB=L63 CSS FUL L64
L66      STR
L67      10896 SEA FILE=REGISTRY SUB=L65 CSS FUL L66
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L68 ( 181680)SEA FILE=REGISTRY ABB=ON  PLU=ON  333.446/RID
L69      STR
L70 ( 56975)SEA FILE=REGISTRY SUB=L68 CSS FUL L69
L71      STR
L72 ( 47535)SEA FILE=REGISTRY SUB=L70 CSS FUL L71
L73      STR
L74 ( 10896)SEA FILE=REGISTRY SUB=L72 CSS FUL L73
L75      STR
L76 ( 10891)SEA FILE=REGISTRY SUB=L74 CSS FUL L75
L77      STR
L78      843 SEA FILE=REGISTRY SUB=L76 CSS FUL L77
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          ACT YOUNG832F/A
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L79 ( 181680)SEA FILE=REGISTRY ABB=ON  PLU=ON  333.446/RID
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L81 ( 56975)SEA FILE=REGISTRY SUB=L79 CSS FUL L80
L82      STR
L83 ( 47535)SEA FILE=REGISTRY SUB=L81 CSS FUL L82
L84      STR
L85 ( 10896)SEA FILE=REGISTRY SUB=L83 CSS FUL L84
L86      STR
L87 ( 10891)SEA FILE=REGISTRY SUB=L85 CSS FUL L86
L88      STR
L89 ( 843)SEA FILE=REGISTRY SUB=L87 CSS FUL L88
L90 ( 744)SEA FILE=REGISTRY ABB=ON  PLU=ON  L89 NOT (PMS OR MNS OR IDS)/C
L91 ( 640)SEA FILE=REGISTRY ABB=ON  PLU=ON  L90 NOT COMPD
L92 ( 582)SEA FILE=REGISTRY ABB=ON  PLU=ON  L91 NOT SQL/FA
L93 ( 75)SEA FILE=REGISTRY ABB=ON  PLU=ON  L92 AND NC>=2
L94 ( 42)SEA FILE=REGISTRY ABB=ON  PLU=ON  L93 NOT MXS/CI
L95 ( 27)SEA FILE=REGISTRY ABB=ON  PLU=ON  L94 NOT 58-61-7/CRN
L96 ( 507)SEA FILE=REGISTRY ABB=ON  PLU=ON  L92 NOT L93
L97 ( 506)SEA FILE=REGISTRY ABB=ON  PLU=ON  L96 NOT 58-61-7
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 L100 444 S L99 NOT (58-55-9 OR 118-00-3 OR 958-09-8)

FILE 'HCAPLUS' ENTERED AT 06:59:20 ON 22 OCT 2002

L101 4269 S L1
 L102 7004 S (G OR GRANULOCYT?) () (CSF OR COLON? STIMULAT? FACTOR)
 L103 7098 S L101,L102
 L104 138 S L2
 L105 52 S (CL OR CI) () IB MECA
 L106 139 S IB MECA
 L107 34 S AB MECA
 L108 1501 S APNEA NOT SLEEP?
 L109 25 S 2 CHLORO () (N6 OR N 6) () 3 IODOBENZ? ADENOSIN? 5 N METHYLURON
 L110 48 S (N6 OR N 6) () 3 IODOBENZ? ADENOSIN? 5 N METHYLURONAMIDE
 L111 49 S (N6 OR N 6) () 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADENOS
 L112 7 S (N6 OR N 6) () 4 AMINO 3 IODOBENZ? ADENOSIN? 5 N METHYLURONAMID
 L113 1 S N 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADENOSIN?)
 L114 49 S (N6 OR N 6) () 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADEN
 L115 0 S 6 N 2 4 AMINOPHENYL () (ETHYLADENOSIN? OR ETHYL ADENOSIN?)
 L116 108 S A3AR OR A2AR OR A3AR
 L117 11994 S ADENOSIN? (L) RECEPTOR?
 E ADENOSINE RECEPTOR/CT.
 L118 2069 S E6,E7,E8,E9,E10
 L119 46 S A2AAR OR A2BAR
 E E5+ALL
 L120 4563 S E8,E7+NT
 L121 4 S L103 AND L104-L115
 L122 18 S L103 AND L116-L120
 E LEUKOPEN
 L123 3002 S E4-E9,E12
 E LEUCOPEN
 L124 1037 S E4-E7,E11
 E LEUKOCYTOPEN
 L125 970 S E2,E4,E5,E8
 E LEUCOCYTOPEN
 L126 28 S E4
 E LEUKOCYTOPEN/CT
 E E4+ALL
 L127 807 S E3
 L128 3392 S E3/BI OR E4/BI OR E5/BI OR E6/BI
 L129 164 S L103 AND L123-L128
 L130 3 S L121,L122 AND L129
 E BONE MARROW/CT
 E E3+ALL
 L131 21852 S E16+NT
 L132 51298 S E16/BI
 E E20+ALL
 L133 31615 S E6+NT
 E E30+ALL
 E E22+ALL
 L134 19391 S E4,E3+NT
 L135 16238 S E3/BI
 E E10+ALL
 L136 22302 S E5+NT
 E E29+ALL
 L137 1555 S E4
 E E13+ALL
 L138 2838 S E5,E6,E4+NT
 L139 9 S L104-L115 AND L123-L129
 L140 13 S L104-L115 AND L131-L138
 L141 129 S L116-L120 AND L123-L128,L131-L138
 L142 5496 S L52,L60,L99

FILE 'REGISTRY' ENTERED AT 07:16:53 ON 22 OCT 2002

L143 10433 S L67,L78 NOT L52,L60,L99
L144 10432 S L143 NOT (58-55-9 OR 118-00-3 OR 958-09-8 OR 58-61-7)
L145 10431 S L144 NOT 53-84-9
L146 2046 S L145 NOT (P/ELS OR SQL/FA OR (PMS OR MNS OR MXS OR IDS)/CI)

FILE 'HCAPLUS' ENTERED AT 07:18:29 ON 22 OCT 2002

L147 5695 S L146
L148 10759 S L142,L147
L149 57 S L148 AND L103
L150 2126 S L148 AND L116-L120
L151 335 S L148 AND L123-L128,L131-L138
L152 18 S L150 AND L151
L153 37 S L149 AND L150,L151
L154 4 S L152 AND L153
L155 36 S L121,L122,L130,L139,L140,L154
L156 53 S L149,L153 NOT L155
L157 114 S L141 NOT L155,L156
E CAN/CS,PA
E CAN-FIT/CS,P
E CAN-FIT/CS,PA
E CAN FIT/CS,PA
L158 7 S E5-E10
E FISHMAN P/AU
L159 86 S E3-E6,E15
L160 6 S L158,L159 AND L103
L161 6 S L160 AND L155-L157
L162 136 S L155-L157 AND (PD<=19990910 OR PRD<=19990910 OR AD<=19990910)
L163 26 S L155 AND L162
L164 6 S L163 AND (HEMATOPO? OR CANCER OR BONE MARROW OR CELL PROLIFER
L165 25 S L162 AND L156
L166 15 S L165 AND (MARROW OR RANDOMIZ? OR MYELO? OR LEUKEM?)/TI
L167 8 S L166 NOT FLAG/TI
SEL DN AN 2 3 5 8
L168 4 S L167 NOT E1-E12
L169 13 S L161,L164,L168
L170 85 S L162 NOT L163-L169
L171 34 S L170 AND (1 OR 15 OR 63)/SC
L172 13 S L171 AND (MAST CELL OR PROLIFERAT? OR HEMATOPO? OR EXPANSION
SEL DN AN 1 3
L173 6 S E3-E18
L174 19 S L169,L173 AND L101-L142,L147-L173
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 07:39:39 ON 22 OCT 2002

L175 11 S E19-E29
L176 1 S L175 AND L1
L177 10 S L175 NOT L176

FILE 'REGISTRY' ENTERED AT 07:40:25 ON 22 OCT 2002

FILE 'HCAPLUS' ENTERED AT 07:40:44 ON 22 OCT 2002

FILE 'REGISTRY' ENTERED AT 07:41:18 ON 22 OCT 2002

FILE 'MEDLINE' ENTERED AT 07:41:38 ON 22 OCT 2002

L178 202 S L104-L107,L109-L115
L179 44 S APNEA AND L178
L180 202 S L178,L179
L181 10611 S L103
L182 3 S L180 AND L181
E RECEPTORS, PURINERGIC/CT
E E3+ALL

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L183      8925 S E12+NT
L184     17516 S ADENOSINE/CT,CN
L185     12727 S L117,L116,L119
L186     12025 S L123-L126
           E LEUCOCYTOP
L187       91 S E4-E6
           E LEUKOCYTOP
L188      518 S E4-E8
           E LEUKOCYTOP/CT
           E E4+ALL
           E E2+ALL
L189     19264 S E5+NT
L190     10323 S E5/BI
           E LEUCOPEN
L191     10566 S E4-E14,E22-E24
L192       1 S E25
           E LEUCOPEN
L193     1483 S E4-E16
L194       0 S L180 AND L187-L193
L195     426 S L181 AND L183-L186
L196     1919 S L181 AND L187-L193
L197     410 S L195 AND L196
L198     112 S L197 AND BONE MARROW
           E BONE MARROW/CT
           E E5+ALL
L199    154734 S E6+NT
           E BONE MARROW/CT
           E E3+ALL
L200     43251 S E4+NT
L201      82 S L197 AND L199,L200
L202     123 S L198,L201 AND PY<=1999
L203      0 S L183-L185 AND L202
L204     632 S L183-L185 AND L199,L200
L205     11 S L183-L185 AND L187-L193
L206     10 S L204,L205 AND L181
L207      4 S L206 AND PY<=1999
L208      3 S L207 NOT MRNAS/TI
           E FISHMAN P/AU
L209     364 S E3-E9,E14
L210      3 S L209 AND L181
L211      4 S L209 AND L180
L212     13 S L209 AND L183-L185
L213      0 S L209 AND L186-L193
L214     41 S L209 AND L199-L200
L215     44 S L210-L214 AND PY<=1999
           SEL DN AN 1 3
L216      2 S L215 AND E1-E6
L217      5 S L208,L216

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FILE 'MEDLINE' ENTERED AT 07:56:20 ON 22 OCT 2002

=> fil biosis

FILE 'BIOSIS' ENTERED AT 07:57:22 ON 22 OCT 2002
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L220 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:391201 BIOSIS
DN PREV200200391201
TI A3 adenosine receptor as a target for cancer therapy.
AU **Fishman, Pnina (1)**; Bar-Yehuda, Sara; Madi, Lea; Cohn, Ilan
CS (1) Laboratory of Tumor and Clinical Immunology, Felsenstein Medical Research Institute, Rabin Medical Center, Petach-Tikva, 49100: pfishman@post.tau.ac.il Israel
SO Anti-Cancer Drugs, (June, 2002) Vol. 13, No. 5, pp. 437-443. <http://www.anti-cancerdrugs.com/>. print. ISSN: 0959-4973.
DT General Review
LA English
AB Targeting the A3 adenosine receptor (A3AR) by adenosine or a synthetic agonist to this receptor (IB-MECA and CI-IB-MECA) results in a differential effect on tumor and on normal cells. Both the adenosine and the agonists inhibit the growth of various tumor cell types such as melanoma, colon or prostate carcinoma and lymphoma. This effect is specific and is exerted on tumor cells only. Moreover, exposure of peripheral blood mononuclear cells to adenosine or the agonists leads to the induction of **granulocyte colony stimulating factor (G-CSF)** production. When given orally to mice, the agonists suppress the growth of melanoma, colon and prostate carcinoma in these animals, while inducing a myeloprotective effect via the induction of **G-CSF** production. The de-regulation of the Wnt signaling pathway was found to be involved in the anticancer effect. Receptor activation induces inhibition of adenylyl cyclase with a subsequent decrease in the level of protein kinase A and protein kinase B/Akt leading to activation of glycogen synthase kinase-3beta, a key element in the Wnt pathway. The oral bioavailability of the synthetic A3AR agonists, and their induced systemic anticancer and myeloprotective effect, renders them potentially useful in three different modes of treatment: as a standalone anticancer treatment, in combination with chemotherapy to enhance its therapeutic index and myelprotection. It is evident that use of the A3AR agonist for increasing the therapeutic index of chemotherapy may also invariably give rise to myelprotection and vice versa. The A3AR agonists are thus a promising new class of agents for cancer therapy.
CC Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
Pharmacology - Clinical Pharmacology *22005
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Hominidae 86215
Muridae 86375
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
1-deoxy-1-[6-[[[(3-iodophenyl)methyl]amino]-9H-purine-9-yl]-N-methyl-beta-D-ribofuranuronamide: A-3 adenosine receptor agonist, antineoplastic - drug; 2-chloro-N-6-(3-iodobenzyl)adenosine-5'-N-methyluronamide: A-3 adenosine receptor agonist, antineoplastic - drug; A-3 adenosine receptor: anticancer drug therapy target, tumor expression
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
HCT-116 cell line (Hominidae): drug treatment, human colon cancer cell

line, in-vivo xenograft study; nude mouse (Muridae): animal model

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman
Vertebrates; Primates; Rodents; Vertebrates

L220 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:577692 BIOSIS
DN PREV200100577692
TI A3 adenosine receptor agonist prevents chemotherapy induced myelotoxicity
via the induction of G-CSF.
AU **Fishman, P. (1);** Ohana, G. (1); Bar-Yehuda, S. (1); Barer, F.
(1)
CS (1) Laboratory of Clinical and Tumor Immunology, Felsenstein Medical
Research Center, Rabin Medical Center, Tel-Aviv University, Petach-Tikva,
49100 Israel
SO International Journal of Molecular Medicine, (2001) Vol. 8, No. Supplement
1, pp. S14. print.
Meeting Info.: 6th World Congress on Advances in Oncology, and the 4th
International Symposium on Molecular Medicine Hersonissos, Crete, Greece
October 18-20, 2001
ISSN: 1107-3756.
DT Conference
LA English
SL English
CC General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and
Reticuloendothelial Pathologies *15006
Pharmacology - General *22002
Pharmacology - Blood and Hematopoietic Agents *22008
Toxicology - General; Methods and Experimental *22501
Toxicology - Pharmacological Toxicology *22504
Toxicology - Antidotes and Preventative Toxicology *22505
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic
Effects *24004
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms
*24010
BC Muridae 86375
IT Major Concepts
Pharmacology; Toxicology; Tumor Biology
IT Diseases
cancer: neoplastic disease; chemotherapy induced myelotoxicity: blood
and lymphatic disease, prevention and control, toxicity
IT Chemicals & Biochemicals
2-chloro-N-6-(3-iodobenzyl)adenosine-5'-N-methyl uronamide: A-3
adenosine receptor agonistic activity, antidote - drug,
granulocyte colony stimulating
factor inducer, hematologic - drug; cyclophosphamide:
antineoplastic - drug, hematologic toxicity; doxorubicin:
antineoplastic - drug, hematologic toxicity
IT Alternate Indexing
Neoplasms (MeSH)
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae): animal model
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;

Rodents; Vertebrates
RN 50-18-0 (CYCLOPHOSPHAMIDE)
23214-92-8 (DOXORUBICIN)

L220 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:513049 BIOSIS
DN PREV200100513049
TI The A3 adenosine receptor as a new target for cancer therapy and chemoprotection.
AU **Fishman, Pnina (1)**; Bar-Yehuda, Sara; Barer, Faina; Madi, Lea; Multani, Asha S.; Pathak, Sen
CS (1) Laboratory of Clinical and Tumor Immunology, Faculty of Medicine, Tel-Aviv University Sackler, Felsenstein Medical Research Center, Rabin Medical Center, Petach-Tikva, 49100: pfishman@post.tau.ac.il Israel
SO Experimental Cell Research, (October 1, 2001) Vol. 269, No. 2, pp. 230-236. print.
ISSN: 0014-4827.
DT Article
LA English
SL English
AB Adenosine, a purine nucleoside, acts as a regulatory molecule, by binding to specific G-protein-coupled A1, A2A, A2B, and A3 cell surface receptors. We have recently demonstrated that adenosine induces a differential effect on tumor and normal cells. While inhibiting in vitro tumor cell growth, it stimulates bone marrow cell proliferation. This dual activity was mediated through the A3 adenosine receptor. This study showed that a synthetic agonist to the A3 adenosine receptor, 2-chloro-N6-(3-iodobenzyl)-adenosine-5'-N-methyl-uronamide (Cl-IB-MECA), at nanomolar concentrations, inhibited tumor cell growth through a cytostatic pathway, i.e., induced an increase number of cells in the G0/G1 phase of the cell cycle and decreased the telomeric signal. Interestingly, Cl-IB-MECA stimulates murine bone marrow cell proliferation through the induction of **granulocyte-colony-stimulating factor**. Oral administration of Cl-IB-MECA to melanoma-bearing mice suppressed the development of melanoma lung metastases (60.8+-6.5% inhibition). In combination with cyclophosphamide, a synergistic anti-tumor effect was achieved (78.5+-9.1% inhibition). Furthermore, Cl-IB-MECA prevented the cyclophosphamide-induced myelotoxic effects by increasing the number of white blood cells and the percentage of neutrophils, demonstrating its efficacy as a chemoprotective agent. We conclude that A3 adenosine receptor agonist, Cl-IB-MECA, exhibits systemic anticancer and chemoprotective effects.

CC Cytology and Cytochemistry - General *02502
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - General *10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Endocrine System - General *17002
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004

BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Tumor Biology
IT Parts, Structures, & Systems of Organisms
bone marrow: blood and lymphatics, immune system; neutrophils: blood and lymphatics, immune system
IT Diseases
cancer: neoplastic disease; melanoma: neoplastic disease
IT Chemicals & Biochemicals
2-chloro-N-(3-iodobenzyl)-adenosine-5'-N-methyl-uronamide: A3 adenosine receptor agonist; A3 adenosine receptor; adenosine; **granulocyte colony stimulating factor**
IT Alternate Indexing

Neoplasms (MeSH); Melanoma (MeSH)

IT Miscellaneous Descriptors
chemoprotection

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
B-16-F10 cell line (Hominidae): melanoma cell line

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 58-61-7 (ADENOSINE)
143011-72-7 (GRANULOCYTE COLONY
STIMULATING FACTOR)

L220 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2000:253371 BIOSIS

DN PREV200000253371

TI Adenosine acts as a chemoprotective agent by stimulating G-CSF production: A role for A1 and A3 adenosine receptors.

AU Fishman, Pnina (1); Bar-Yehuda, Sara; Farbstein, Tamar; Barer, Faina; Ohana, Gil

CS (1) Laboratory of Clinical and Tumor Immunology, Rabin Medical Center, The Felsenstein Medical Research Institute, Petach-Tikva, 49100 Israel

SO Journal of Cellular Physiology, (June, 2000) Vol. 183, No. 3, pp. 393-398. print..
ISSN: 0021-9541.

DT Article

LA English

SL English

AB Adenosine, a ubiquitous nucleoside, is released into the extracellular environment from metabolically active or stressed cells. It binds to cells through specific A1, A2A, A2B and A3 G-protein-associated cell-surface receptors, thus acting as a signal-transduction molecule by regulating the levels of adenylyl cyclase and phospholipase C. In this study, we showed that adenosine stimulates the proliferation of murine bone marrow cells in vitro. Pharmacological studies, using antagonists to the adenosine receptors, revealed that this activity was mediated through the binding of adenosine to its A1 and A3 receptors. This result was further corroborated by showing that the two selective A1 and A3 receptor agonists, N-cyclopentyladenosine (CPA) and 1-deoxy-1-(6-((3-iodophenyl)methyl)amino)-9H-purin-9-yl)-N-methyl-beta-D-ribofuranuronamide (IB-MECA) respectively, induced bone marrow cell proliferation in a manner similar to adenosine. Adenosine's interaction with its A1 and A3 receptors induced G-CSF production, which led to its stimulatory effect on bone marrow cells. These results were confirmed in vivo when we demonstrated that low-dose adenosine (0.25 mg/kg) acted as a chemoprotective agent. When administered after chemotherapy, it restored the number of leukocytes and neutrophils to normal levels, compared with the decline in these parameters after chemotherapy alone. It is suggested that low-dose adenosine, already in clinical use, may also be applied as a chemoprotective agent.

CC Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Endocrine System - General *17002
Immunology and Immunochemistry - General; Methods *34502

BC Muridae 86375

IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis)

IT Parts, Structures, & Systems of Organisms
A1 adenosine receptors; A3 adenosine receptors; bone marrow cells: blood and lymphatics, immune system

IT Chemicals & Biochemicals

adenosine: chemoprotective agent; **granulocyte colony stimulating factor**: production stimulation

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae): animal model, male

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates

RN 58-61-7 (ADENOSINE)
143011-72-7 (GRANULOCYTE COLONY STIMULATING FACTOR)

L220 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1999:191711 BIOSIS

DN PREV199900191711

TI Adenosine acts as a chemoprotective agent: A new mechanism.

AU **Fishman, P.**; Bar-Yehuda, S.; Farbstein, T.; Bahaar, F.

CS Felsentein Med. Res. Cent., Sackler Fac. Med., Tel Aviv Univ., Rabin Med. Cent., Petah Tikva 49100 Israel

SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 677.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.

DT Conference

LA English

CC Pharmacology - General *22002
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - General *10060
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Immunology and Immunochemistry - General; Methods *34502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520

BC Hominidae 86215
Muridae 86375

IT Major Concepts
Pharmacology

IT Parts, Structures, & Systems of Organisms
bone marrow cell: blood and lymphatics, immune system

IT Chemicals & Biochemicals
adenosine: chemoprotective agent; A1 adenosine receptor; G-
CSF [granulocyte-colony stimulating factor]

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae); murine (Muridae)

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

RN 58-61-7 (ADENOSINE)



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3	LET.	1

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